PROSPECTIVE STUDY ON HAEMATOLOGICAL AND COAGULATION CHANGES IN ACUTE PANCREATITIS

Dissertation submitted in partial fulfilment of the requirements for the award of the degree of

DM (MEDICAL GASTROENTEROLOGY)

BRANCH - IV

of

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI, INDIA.

MADRAS MEDICAL COLLEGE,

CHENNAI 600003

August 2013

DECLARATION

I solemnly declare that this dissertation titled "**Prospective study on haematological and coagulation changes in Acute pancreatitis**" is done by me in the Department of Medical Gastroenterology,Madras Medical college & Rajiv Gandhi Government General Hospital,Chennai under the guidance and supervision of Professor & Head of the Department ,Department of Medical Gastroenterology,Madras Medical College & Rajiv Gandhi Government General Hospital,Chennai.This dissertation is submitted to the Tamilnadu Dr.MGR Medical University ,Chennai in partial fulfilment of the university requirements for the award of the degree of DM Medical Gastroenterology.

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CERTIFICATE

This is to certify that the dissertation entitled "**PROSPECTIVE STUDY ON HAEMATOLOGICAL AND COAGULATION CHANGES IN ACUTE PANCREATITIS."** is the bonafide work done by **Dr. SHAFIQUE.A**,under our guidance and supervision in the Department of Medical Gastroenterology, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai submitted as partial fulfilment for the requirements of D.M.Degree examination Branch IV MEDICAL GASTROENTEROLOGY,AUGUST 2013,under The Dr.M.G.R.Medical University ,Chennai.

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ACKNOWLEDGEMENT

I sincerely thank the Dean, **Prof. Dr. V.KANAGASABAI M.D.,** Dean, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 for having permitted me to use hospital resources for the study.

I have great pleasure in expressing my gratitude and respect to **Prof.Dr.MOHAMMED ALI M.D.D.M**,Professor and Head of Department of Medical Gastroenterology, Madras Medical College ,Chennai, for his valuable suggestions, kind guidance, constant supervision and moral support ,without this study would not have been possible.

I have great pleasure in expressing my gratitude and respect to **Prof.Dr.T.PUGHAZHENDHI,M.D.,D.M.**,Additional Professor,Department of Medical Gastroenterology, , Madras Medical College for his valuable guidance and constructive suggestions.

I express my heartfelt gratitude to **Dr.T.Usha** ,Associate Professor, Department of Haematology, Madras Medical College, Chennai for her able guidance without whom this study is not possible.

I express my gratitude to assistant professors, **Dr.K.Premkumar, Dr.Caroline, Selvi.Dr.Ratnakhar Kini, Dr.Kani Sheik Mohammed** for their support, interest and enthusiasm in completion of this study.

I thank my colleagues, **Dr T.K.Anand, Dr.M.Radha, Dr.Arvind M.A, Dr.Hemamala, Dr.P.Senthilkumar** for their help and assistance in successfully completing the study.

I express my sincere gratitude to all the patients who participated in the study.This work would be complete if it had contributed ,even in the smallest possible way ,to alleviate their suffering.

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ABBREVIATIONS

APTT	-	Activated partial thromboplastin time
PT	-	Prothrombin time
INR	-	International Normalised ratio
FDP	-	Fibrinogen Degradation Product
AP	-	Acute pancreatitis
APACHE	-	The Acute Physiology and Chronic Health evaluation
CRP	-	C- reactive protein
CT	-	Computerised Tomography
USG	-	Ultra sonogram
ASA	-	Aminosalyclic acid
ERCP	-	Endoscopic retrograde Cholongio pancreatography
BISAP	-	Blood urea nitrogen/Impaired mentalstatus/SIRS score/Age/pleural effusion.
IL	-	Interleukins
CTSI	-	Computerised tomography severity index.
TF	-	Tissue factor
Vwf	-	Vonwillibrand factor.
SIRS	-	Systemic inflammatory response syndrome
DIC	-	Disseminated Intrvascular coagulation
PAI	-	Platelet activator inhibitor.
ISTH	-	International society on thrombosis and haemostasis.
APC	-	Activated Protein C
MMP	-	Matrix metalloproteinase

INTRODUCTION

Acute pancreatitis was defined in the Atlanta symposium as an acute inflammatory process involving the pancreas that further involve peripancreatic tissues and organs remote from the pancreas. Criteria had been defined for severity which include organ failure (Pulmonary insufficiency,shock and renal failure) and /or complications involving locally which include pseudocyst.pancreatic necrosis and pancreatic abscess[41] .

The diagnosis of the disease requires 2 out of the following 3 features[43]: 1) Abdominal pain characteristic of acute pancreatitis.2) serum amylase and /or lipase which is ≥ 3 times the upper limit of normal and 3) characteristics findings in Imaging (USG/CT scan).The severity of acute pancreatitis does not correlate with the rise in level of serum lipase and amylase.Risk factors of severity of acute pancreatitis at admission include older age,obesity and organ failure.

Tests at admission which distinguish mild from severe acute pancreatitis include APACHE-11 score(≥8-suggestive of severe AP) and serum haematocrit (<44 suggests mild acute pancreatitis). A high CRP level measured within 72hours correlates with formation of pancreatic necrosis. Pancreatic necrosis and persistent organ failure were the most important factors responsible for severity in acute pancreatitis[29].The most important

investigation to distinguish interstitial from necrotizing type of acute pancreatitis is CECT abdomen and it is more sensitive and specific especially if taken 2-3 days after the onset of illness. Mortality rate increases to >40% when the multisystem organ failure coexistent with necrotizing type of acute pancreatitis.

The commonest etiological factors observed in AP were Chronic Alcohol abuse and Gallbladder stones[11]. They comprise about 80% of all cases (Forsmark et al 2007). Around 10% of the cases, the cause was unknown (Tonsi et al 2009). Some other causes of Acute pancreatitis were hypercalcemia, hypertriglyceridemia, trauma, drugs like methyldopa, 5-ASA, L-asparginase, scorpion sting, duodenal diverticula,parasites,annular pancreas, choledochocele, infections (coxackie,measles, mycoplasma, leigonella, leptospira, salmonella and tuberculosis) , hereditary , autoimmune causes ,tumors ,endoscopic retrograde cholangiopancreatography (ERCP) and developmental abnormalities.

The Theory behind the pathogenesis of acute Pancreatitis was proposed as acinar cells injury, which in turn leads into pancreatic enzymes leakage into pancreatic tissue. These enzymes get activated and initiate the process of auto digestion [19]. The proteases which were activated ie., elastase,trypsin and

lipase breaks down cell membranes and tissues which in turn causes vascular damage, oedema,, haemorrhage and necrosis.

The development of acute necrotizing pancreatitis is usually associated with pancreatic glandular necrosis. Acinar cell apoptosis, the release of cytokines, activation of coagulation, tissue ischemia, and tissue necrosis are key factors in the progression of the condition[38], as well as in the development of associated extrapancreatic complications. (Steinberg & Tenner, 1994; McKay & Buter, 2003; Pandol et al., 2007).

Atlanta classification divided acute pancreatitis into two broad categories[36,41]

Mild Acute Pancreatitis :(edematous and interstitial)

It was defined as pancreatitis associated with minimal organ dysfunction and an uneventful recovery.

Severe Acute pancreatitis :(necrotizing) [42].

Criteria for severe acute pancreatitis included any of the following:

A Ranson's score of 3 or more and /or an APACHE11 score of 8 or more within the first 48hours , Organ failure (respiratory,circulatory,renal and

/or gastrointestinal bleeding) and /or local complications(pancreatic necrosis, abscess or pseudocyst).

Predictive marker for severity[37] :

Clinical assessment,clinicophysiological scoring systems, imaging techniques and biochemical markers.

There are Prognostic system criteria for assessing severity including Atlanta severity criteria, Ranson's criteria ,Glasgow score, APACHE11 score, SIRS score, recent severity score like BISAP score, Panc 3 score, Japanese severity score, Harmless acute Pancreatitis Score and artificial network scores. Apart from these, Biochemical scores like C- reactive Protein, Procalcitonin, Serum Amyloid A, Trypsinogen Activation Peptide, Polymorphonuclear Granulocyte Elastase, Interleukins IL-6&MCP-1,Hematocrit and BUN [28].

In spite of all these clinical & biological markers ,There is yet no single marker could serve as an optimal predictor of disease severity in acute pancreatitis[48].

Hence imaging methods like ultra sonogram ,computed tomography, Echo – enhanced ultrasound,Magnetic Resonance Imaging been tried to assess the severity of acute pancreatitis.

Of the imaging methods Contrast enhanced CT scan abdomen is currently the best imaging method recognised for assessment of severity in acute pancreatitis. Balthazar and his co-workers formulated a new index called as CT severity index(CTSI) which showed a good correlation with the clinical parameters in patients with acute pancreatitis.

CT grade as per Balthazar score [35]

A - normal

B - focal or diffuse enlargement of the pancreas, including irregularities of contour and inhomogeneous attenuation;

C - pancreatic gland abnormalities in B plus peripancreatic inflammation;

D - grade C plus a single fluid collection;

E - grade C plus 2 or more fluid collections and /or the presence of gas in or adjacent to pancreas.

This index scores the degree of pancreatic inflammation and necrosis on a scale with a maximum of 10points.Patients with a severity index of 0-1 exhibited no morbidity or mortality, whereas 4% morbidity rate and no mortality rate were seen with CT severity index of 2. In contrast, patients with a CT severity index of 7-10 yielded 92% morbidity and 17% mortality rate[39].

Mortele et al modified the CTSI by introducing extrapancreatic complications(Pleural effusion,ascites,vascular and GI complications)

Modified CT Severity Index[34]

Prognostic Indicator	Points
Pancreatic inflammation	
Normal pancreas	0
Intrinsic pancreatic abnormalities with/without inflammatory changes in peripancreatic fat	2
Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis	4
Pancreatic necrosis	
None	0
<30%	2
>30%	4
Extrapancreatic complications	
One or more of pleural effusion,ascites,vascular complications,parenchymal complications,or gastrointestinal involvement.	2

The Haematological and coagulation parameters were assessed in the study population and these indices are correlated with the severity of disease which was defined by the above CT Severity Index criteria.

AIM OF THE STUDY

To Study the Haematological and coagulation changes prospectively in patients with acute pancreatitis and correlating the changes to its severity.

REVIEW OF LITERATURE

Haematological and coagulation abnormalities in acute pancreatitis were noted in literature studies [1].

Trapnell (1966)in his study reported falls in values of hemoglobin, white blood cell count and haematocrit in acute pancreatitis patients[9].

Innerfield, Angrist and Benjamin (1952) noted a state of hypocoagulability, whereas other workers have observed a hypercoagulable state. (Shinowara et al., 1963)[8].

Disseminated intravascular coagulation (DIC) has been observed in acute pancreatitis[4] (Minna, Robboy and Colman, 1974; Yoshikawa, Tanaka and Guze, 1971) and post-mortem studies also have confirmed the presence of widespread thrombosis in a proportion of cases.(Smyth, 1940).

Desmond Murphy and Clement W.Imrie in their study showed fall in Hemoglobin (48%) and Haematocrit (88%) of their patients. They also showed reticulocytosis in 22% of their patients.

The fall in hemoglobin and haematocrit may be caused by a combination of hemodilution ,intravascular coagulation and blood loss into and around the pancreas[1], and also been noted previously(Trapnell,1966).

Gastric erosions, acute peptic ulceration and bleeding into the pancreatic tissues or a pseudo-cyst, are usually considered the major causes of a falling hemoglobin in patients with acute pancreatitis, and this additional cause must be kept in mind.

Leucocytosis has been observed in patients with AP and has been related to the more severe form of the disease.

Normal Haemostasis:

Haemostasis normally involve endothelial cells and vessel wall and soluble plasma proteins like coagulation proteins with their regulators, cellular components in blood which included, platelets ,RBC and leukocytes[21]. It also include microparticles derived from leukocytes and platelets.. This is a physiologic process which has the capacity to produce a haemostatic plug outside a damaged blood vessel and also controls the fluidity of blood.

Thrombosis was yet another event which takes place inside the lumen of the vessel , consists of following events which include [22]

a) accumulation of platelets,
b) activation,
c) adhesion of platelets
d) aggregation of platelets

e) and fibrin formation preceded by TF-initiated thrombin generation.

Thrombin formation along with coagulation of blood occurring in vascular damaging site, is induced by platelets which were adherent to vessel wall. The haemostatic process was counter-balanced by anticoagulant mechanisms in normal individual which ensure the regulation of haemostatic effect. In pathological states (e.g. in systemic inflammation), the haemostatic events escapes the control mechanism ,leading to thrombosis.

Coagulation Model :

Years before, the coagulation model was proposed which was called "cascade model" and it was classified into intrinsic and extrinsic pathways, and the common pathway was united at the factor X level. (Macfarlane 1964,Davie and Ratnoff 1964;) This model proposed that coagulation of blood involves a series of calcium-dependent conversions of proenzymes to the serine proteases .[26.]This event converts prothrombin into thrombin (Dahlback 2000).

The extrinsic pathway which occurs after the vascular damage, where in the tissue factor is exposed to the circulation which binds and transfers factor VII to FVIIa. The TF-FVIIa forms a complex and this complex is responsible for activating FIX to FIXa and FX to FXa[33].

The intrinsic pathway involves factor XII contact activation and it occurs only in the presence of HMWK and prekallikrein . The FXIIa is responsible for activation of factorXI to XIa. This event further activates factor IX to IX a. Finaly FIXa activates both factor VIIIa and factor X.

The common pathway involves both FXa and Factor Va by forming a prothrombinase complex, thereby causing conversion of prothrombin to thrombin which in turn converts fibrinogen to fibrin[30]. The contribution of platelets was considered to be an independent mechanism in primary hemostasis. APTT measures the intrinsic pathway whereas PT measures the extrinsic pathway and these 2 tests were important in hemostasis .

Platelets role in acute pancreatitis:

The platelet plug intermingled with the fibrin meshwork forms the thrombus formation . Fibrinogen and Von Willi brand factor (VWF) initiates the adhesion of platelets of vascular injury site. These factors are important for the propagation and amplification phases of coagulation[12]. These factors provide a surface of the damaged area which lies in close proximity.The elements for coagulation were situated in that area.Vascular damage expose the collagen which in turn activate the platelets and formation of thrombin. Studies have shown that in acute pancreatitis, platelets were activated , and hence their indices were altered along with some functional changes[31].

Evidence of increased platelet activation associated with pancreatitis has long been established in experimental animal models. In rabbits, administration of pancreatic fluid from patients with chronic pancreatitis induced platelet aggregation and activation (Prinz et al., 1984). In cases of acute pancreatitis, activated platelets along with indices ie., Platelet large cell ratio, platelet mean volume and distribution width have also been shown to be elevated between onset and remission of AP(Mimidis et al., 2004).

While a heightened platelet response is typical of patients with mild AP, a decreased platelet count (due to increased consumption of platelets) is observed in cases of severe AP[49]. Low plasma levels of platelets in patients with AP are also associated with poor clinical outcome(Maeda et al., 2006).

DIC is a condition which is acquired by intravascular fibrin deposition and microvascular thrombosis following a systemic activation of coagulation[2]. Bleeding occurs due to increased consumption of coagulation factors and platelets .The organ failure occurs due to vascular thrombosis[32].

DIC is associated with conditions like malignancy, hepatic failure, immunological/toxic reactions, vascular abnormalities and organ failure conditions like severe acute pancreatitis. DIC is of two types[6]. The first type is visible one which can be detected by clinical and laboratory method. The other one is invisible which can not be detected by clinical and laboratory method[51].

The former one is more dangerous as it indicates a decompensated hemostatic system[2]. Sepsis and Trauma were the commonest condition leading to DIC in 30% and 50% respectively[10], which further increases the death risk in these patients.

Studies have shown that activation of pancreatic enzymes do have role in pathogenesis of Disseminated intravascular coagulation.[5]

The effects of DIC were natural anticoagulant system suppression, fibrinolytic system suppression due to increased level of PAI-1 and there was increase in production of fibrin[2,6] .Thus all anticoagulant mechanism were suppressed during the course of DIC[6].

ISTH Diagnostic Scoring System for DIC

Risk assessment: Does the patient with underlying disorder known to be associated with overt DIC?

- If yes proceed further
- If not, don't use this algorithm.

Order global coagulation tests (PT, platelet count, fibrinogen, D-dimer)

Score the test results:

- Platelet count (>100 k/μL = 0, <100 k/μL = 1, <50 k/μL = 2)
- Elevated D-dimer (<0.4 μg/mL = 0, 0.4–4.0 μg/mL = 2, >4.0 μg/mL=3)

- Prolonged PT (<3 sec = 0, >3 sec but <6 sec = 1, >6 sec = 2)
- Fibrinogen level (>100 mg/dL = 0, <100 mg/dL = 1)

Calculate score:

- If ≥5, compatible with overt DIC: Repeat score daily.
- If <5, suggestive (not affirmative) for nonovert DIC: Repeat next 1–2 days.

Coagulative disturbances in acute pancreatitis :

Accelerated fibrinolysis and consumptive coagulopathy are the known coagulation abnormalities that can occur in severe AP and they are related to organ failure[3,7].

Perfusion and hypoxia of pancreatic organ plays vital role in formation of pancreatic necrosis[46].There are several studies which states that micro vascular abnormalities like inadequate perfusion,shunting,vasoconstriction and increased blood viscosity are responsible for progression of AP[7]. Pancreatic tissue blood flow is another factor when it gets reduced, is a marker of severe AP[47].

Blood coagulation parameters such as activated partial thromboplastin time and prothrombin time measures the intrinsic and extrinsic coagulation pathways respectively. Studies have shown that an elevated prothrombin time

in patients with AP (Radenkovic et al., 2009). However, there have been no reports of significant alterations in partial thromboplastin time (APTT) levels in these patients. with AP [3]. While these measurements suggest some early haemostatic disturbances of AP, their usefulness in predicting patient outcome is questionable. Clinical studies which measure other parameters (most notably FDP and antithrombin) have demonstrated an improved specificity and sensitivity in predicting outcome for these parameters than PT or APTT.

Sawa et al in his study have shown that Plasma TF[23] had higher value when compared with normal volunteers in severe AP, but the difference is not statistically significant.

Plasma levels of TF in alcoholic severe AP[27] with pancreatic necrosis was significantly higher than that in alcoholic severe AP without pancreatic necrosis or that in nonalcoholic severe AP with pancreatic necrosis. These findings suggest that an increase in plasma TF may be related to the development of pancreatic necrosis in alcoholic severe AP[44].

Markedly elevated plasma fibrinogen levels,elevated FDP levels are consistent with intravascular coagulation although they may be interpreted as a non-specific reaction to injury[40].These changes have been noted previously in acute pancreatitis and these changes were attributed to a hypercoagulable

state (Shinowara et al., 1963; Hirayama et al., 1974; Mungall and Hague, 1975).

The Other possible explanations for elevated FDPs in patients with acute pancreatitis include obstructive jaundice, liver disease, pulmonary embolus and venous thrombosis (Merskey et al., 1966) or local haemorrhage (Malleson, 1974).

Therapeutic approach in modulating hemostasis in AP :

Recombinant Drotrecogin alpha activated was the first biological agent studied in improving survival in patients with severe sepsis[15]. Activated Protein C was used as a cytoprotective signaling molecule involved in apoptosis, inflammation and vascular permeability[17]. This was first studied in rat model and it was shown to result in significant decreases in serum IL-8,TNF levels and MMP-9, an enzyme which degrades extracellular matrix components in larger range[18]. Coagulopathy in severe AP was characterized by significantly prolonged APTT and PT, marked leukocytosis, and thrombocytopenia, decreased fibrinogen levels which were not significant in Treated versus untreated APC rats. Alsfasser et al., 2006; Chen et al., 2007 and Yamanel et al., 2005 have shown survival benefit in various models in AP after the success of rat model.

Chen et al., 2007 in his Study have demonstrated good efficacy when treated with high bolus APC injections and also Alsfasser et al demonstrated infusion in hourly basis in 2006[45].Some studies suggested that APC doesn't offer any survival benefit in early phase Acute pancreatitis[14]. When APC was used in lower dose of 24 ug/kg, it offers no therapeutic benefit compared with APC bolus ie., 100 ug/kg or hourly regimen[24].

Platelet activating factor (PAF) modulation had been studied in experimental acute Pancreatitis[25]. In trypsin injection and sodium taurodeoxycholate models, Platelet activating factor is released into the bloodstream peritoneal fluid, of rats[13]. PAF inhibition with an antagonist accelerate its degradation and causes decrease inflammation resulting in reductions in pro-inflammatory cytokines .

Andersson et al., 2007 in his study describe the usage of novel FVIIa inhibiting agent which was investigated in an intraductal taurodeoxycholate infusion model of AP[16] .

Administration of and N-acetylcysteine and activesite inactivated FVII given 90 minutes prior to AP induction causes a reduction in MPO levels in distant organs like ileum and lungs and also reductions in plasma IL-6 levels compared to saline which acts as controls when it occurs 6 hours after acute pancreatitis induction.

Bleeker et al in 1992 demonstrated that high dose Anti Thrombin -lll had been tried in taurocholate induced pancreatitis in rat model [20]which had shown that there was improvement in survival rate. But Anti thrombin was found to be ineffective in improving mortality[20] in critically ill acute pancreatitis patients.

MATERIALS AND METHODS

Study Centre:

Department of Medical Gastroenterology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai

Duration of the Study:

1year

Study Design:

Prospective

Sample Size:

50 cases

Inclusion Criteria:

Patients who are admitted in Department of Medical and surgical Gastroenterology and those patients admitted in other Medical and surgical wards with History and investigations suggestive of Acute pancreatitis.

Exclusion Criteria:

- Patients not willing for study.
- Patients with known Haematological disorders.
- Patients with pre-existing or coexisting Chronic liver disease
- Pregnancy/Postpartum

- H/o surgery in recent past
- Post ERCP pancreatitis
- Post infectious pancreatitis.

Patient selection and Data collection:

50 patients with clinical features of abdominal pain characteristic of acute pancreatitis ,serum amylase and /or lipase≥3times upper limit of normal and CT scan showing characteristic features of acute pancreatitis were chosen and their Haematological and coagulation indices were studied prospectively over a period of 1 year.

Methods:

Detailed clinical history of all 50 patients and thorough physical examination of all 50 patients have been done.

Serum amylase/Lipase was done for all patients.

Liver function tests,Renal function tests,Xray chest PAview,Ultra sonogram abdomen and contrast enhanced CT abdomen were done for all patients to rule out various complications associated with acute pancreatitis.

Etiological workup was done for all 50patients with relevant investigations.

Patients were grouped into mild and severe pancreatitis by using Balthazar CT scoring system and Modified CT severity index score.

Mild Pancreatitis – Balthazar CT score Grade- A,B,and C/ CT SI index≤6

Severe Pancreatitis - Balthazar CT score Grade –D and E,CTSI≥7

Presence of pleural effusion either unilateral or bilateral by chest radiograph or CT scan correlates with severe pancreatitis. Haematological and coagulation parameters are assessed for all patients .

Haematological indices :

1) Complete blood count which includes

   Haemoglobin in gms%

   Haematocrit in %

   Total white blood cell count /cells in cu.mm

   RBC count in millions/cu.mm

   Differential count in %

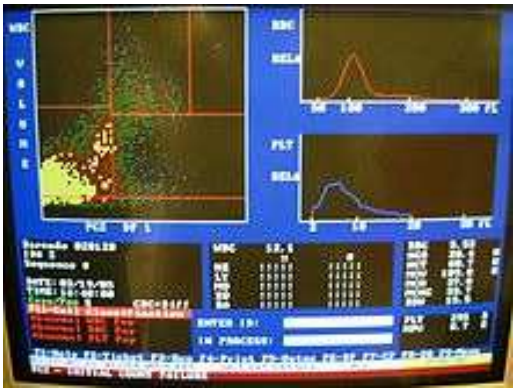
   ESR in mm/hr

   Platelet count in cu.mm

   Method of examining CBC :

   Blood was drawn in EDTA containing test tube to prevent clotting.

Automated haematology analyzer[50]:



Blood taken for examination is mounted on a rack after adequate mixing. Different elements of the blood were analyzed by different components of the instrument. Number and different cell types were analyzed by cell counting compartment .Finally the computer review the results.

These analyzer machines aspirate only small volume of blood. Aspiration is done through narrow tubing where sensors for counting the number of cells located. These sensors can pick up the type of blood cells[50].

Apart from counting and analyzing the white blood cells, Red blood cells and platelets, these analyzers also measure the haemoglobin concentration in blood and also within red blood cells.

1) Haematocrit :

The ratio of volume of erythrocyte to that of whole blood. It is expressed in Percentage. The HCT may be measured directly by centrifugation

with macromethods or micromethods, or indirectly as the product of the mean corpuscular volume (MCV) times RBC count in automated instruments[52]. Here the automated method is used.

2) Reticulocyte count : automated method.

Reticulocyte fractions are separated based on RNA content, with the more immature cells containing the highest amount of reticulum. The immature reticulocyte fraction (IRF) quantitatively describes the youngest reticulocytes with the greatest staining intensity[50].

It involves addition of stain such as new methylene blue and oxazine to detect the RNA content of RBC.

3) Peripheral smear :

Steps : Examination of Wet preparation

Making and stain blood films-Polychrome methylene blue and eosin (Wright's) stain commonly used.

Coagulation Parameters :

Bleeding time and clotting time

Duke process of Bleeding time estimation

The patient was pricked, preferably on the ear finger tip or ear lobe with a lancet , after alcohol swabbing . The prick should be roughly around

3–4 mm deep. Then with help of filter paper ,blood is wiped every 30seconds. The test comes to an end when bleeding stops. The normal Bleeding time is around 2–5 minutes[52].

Clotting time:

5ml of blood is placed in a glass container, kept at body temperature and observed .Normal clotting should occur in 5-15mts.

PT/INR :

Tissue thromboplastin (recombinant human or isolated animal tissue factor) and patient plasma were incubated for several minutes, after which the citrated plasma mixture is recalcified by the addition of excess $CaCl_2$, and the time required for clot formation is measured. The time to fibrin strand formation is then measured automatically by photo optical device[50].

The PT serves as the basis for the international normalized ratio (INR) value which is used to monitor patients on warfarin. The INR is the ratio of patient PT divided by geometric mean normal PT for the local laboratory (based on a population of normal individuals assessed with identical reagents,sample collection and machines), which is raised to the power of the international sensitivity index. Although the INR is clearly the most appropriate measure used in conjunction with oral anticoagulant monitoring, for nonwarfarinized patient, actual PT values can also be used. In our study

both PT and INR are used and INR is used in analysis with normal ratio of 0.9-1.2[52]. The PT measures the extrinsic coagulation pathway of coagulation, which consists of activated FVII (FVIIa) and TF and proteins of the common pathway (factors X, V, II, and fibrinogen)

Activated partial thromboplastin time :

A mixture of a negatively charged surface, phospholipid, and anticoagulated patient plasma(3.2 g% sodium citrate) was incubated for several minutes.. When whole blood is taken, the ratio of anticoagulant to whole blood was 1 part anticoagulant to 9 parts whole blood. Patient's plasma is incubated with the above mixture for a particular time. Then the sample was added with excess calcium chloride, and the clot formation time is measured[52]. The APTT assesses the coagulation proteins of the so-called intrinsic system and common pathways. This assay was commonly referred to as the partial thromboplastin time (PTT), but it was actually an "activated" PTT, in that its reagents contain a negatively charged surface which accelerates the rate of the reaction. The APTT measures proteins of the intrinsic coagulation system (FXII, prekallikrein, ,HMWK, FXI, FIX, and FVIII) and proteins of the common pathway (fibrinogen,factors X, V,and II)[52].

Fibrinogen :

Whenever the reason for prolongation of APTT or PT could not be explained by any means, measurement of fibrinogen level is a valuable tool in identifying the bleeding tendency.

- Fibrinogen assay can be 4 methods
- Clauss
- PT- derived Fibrinogen assays
- Immunological
- Gravimetric assays.

Clauss assay :

Procedure :

Reference plasma with known level of fibrinogen is calibrated with a international standard in a series of dilution and a curve is constructed to create a range of fibrinogen concentration .After that for each of the dilution, clotting time is established and this is plotted on a log graph.When the concentration is 1:10,it is equivalent to 100%[50].

Thrombin and phospholipids are added to diluted plasma which is deficient in platelets after adding up of calcium and incubated at temperature of 35-37degree centigrade . The time taken for clot formation after adding up

of calcium is compared with the curve and fibrinogen concentration is deducted from that.

Fibrinogen degradation Product :

It is the protein fragment formed by the enzymatic reaction of plasmin over fibrinogen and fibrin. It aids in detecting the degree of intravascular coagulation. It also detect fibrinolysis when there is dissolution of fibrin in clot[50].

Test is done using **latex agglutination assay**.

Whole blood should be drawn into tube with Thrombin/Soybean trypsin inhibitor for measuring this assay.

All these parameters were analysed with respect to severity of AP.

Data obtained by above methods were analysed by

1. SPSS 15
2. Chi square tests.

- Ethical committee approval obtained.

OBSERVATIONS & RESULTS

Evaluation of the study subjects :

Observation:

The study subjects were evaluated according to their age and sex distributions related to acute pancreatitis.

Table -1 Sex distribution :

Sex	Frequency	Percent
Male	44	88.0
Female	6	12.0
Total	**50**	**100.00**

The above table-1 shows 88% of acute pancreatitis patients were males when compared to 12% in females .

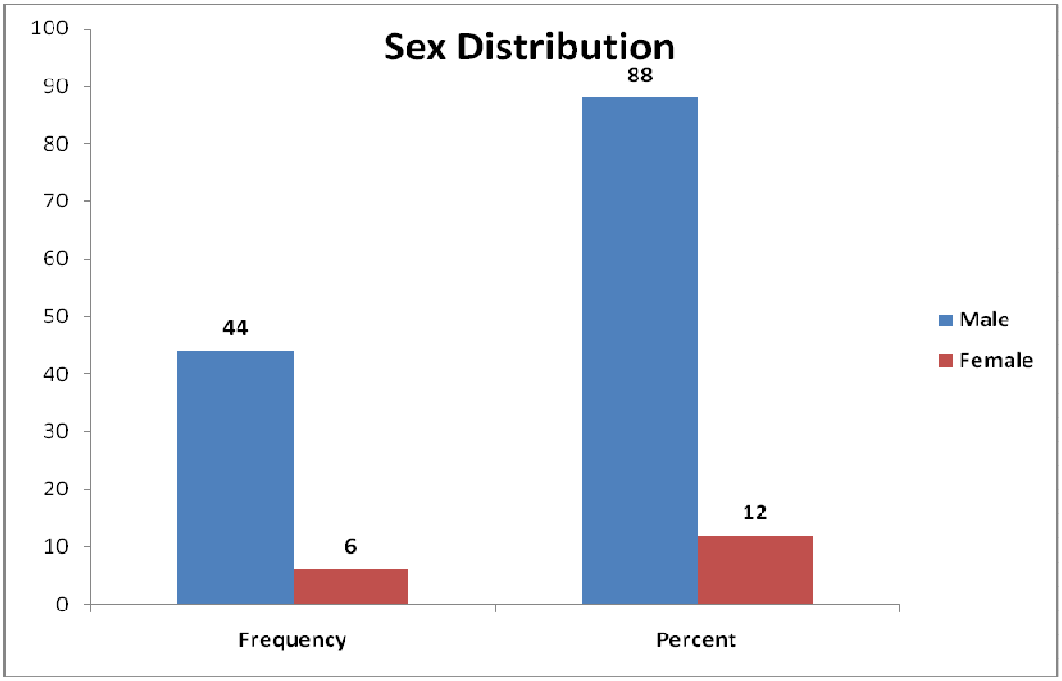


Table 2 - Age wise distribution of study subjects:

Age (Yrs)	Frequency	Percent
11-20	4	8.0
21-30	14	28.0
31-40	21	42.0
41-50	7	14.0
Above 50	4	8.0
Total	**50**	**100.0**

The above table -2 shows 42% of acute pancreatitis in 31-40 age group and 28% in 21-30 group. Rest of age group form just 30% in this study population.

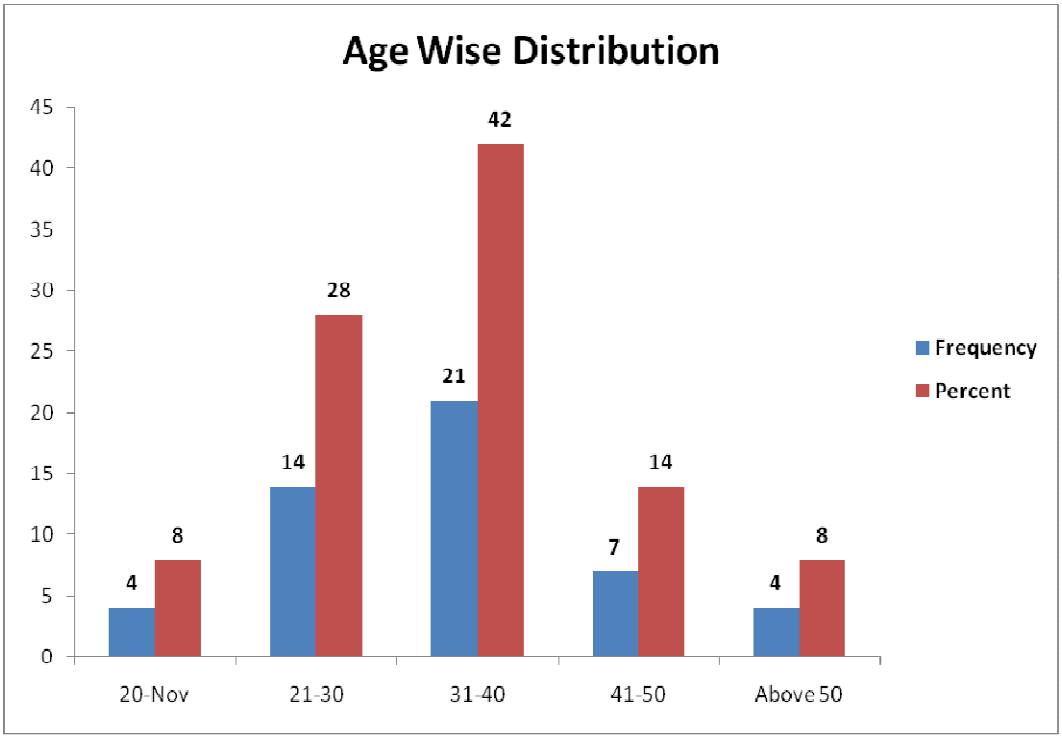


Table 3 :Etiology wise distribution of study subjects:

Etiology	Frequency	Percent
Alcohol	30	60.0
Gallstones	6	12.0
Hyper TGL	2	4.0
Idiopathic	12	24.0
Total	**50**	**100.0**

Table3 shows majority of patients were alcoholic (60%) in this study followed by idiopathic group (24%) and gallstones(12%).

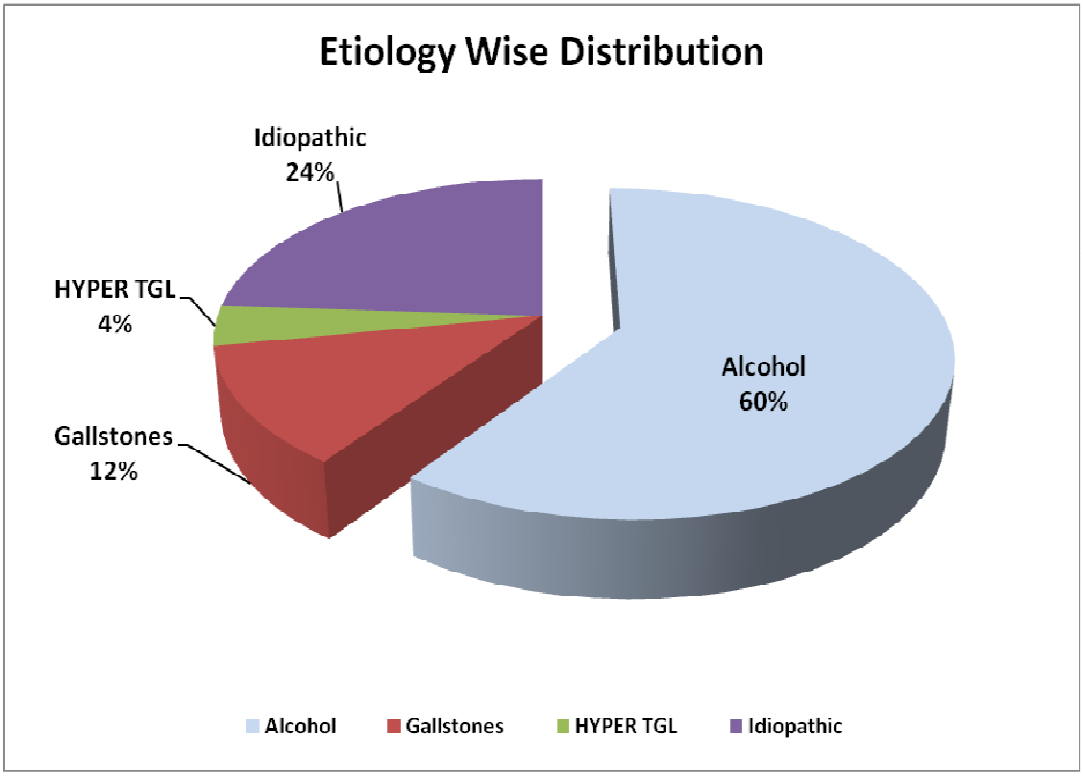


Table 4 : Grade wise distribution of study subjects :

Grade of Severity	Frequency	Percent
Mild	18	36.0
Severe	32	64.0
Total	**50**	**100.0**

Table 4 shows 64%% of study subjects were in severe group and 36% in mild group of acute pancreatitis.

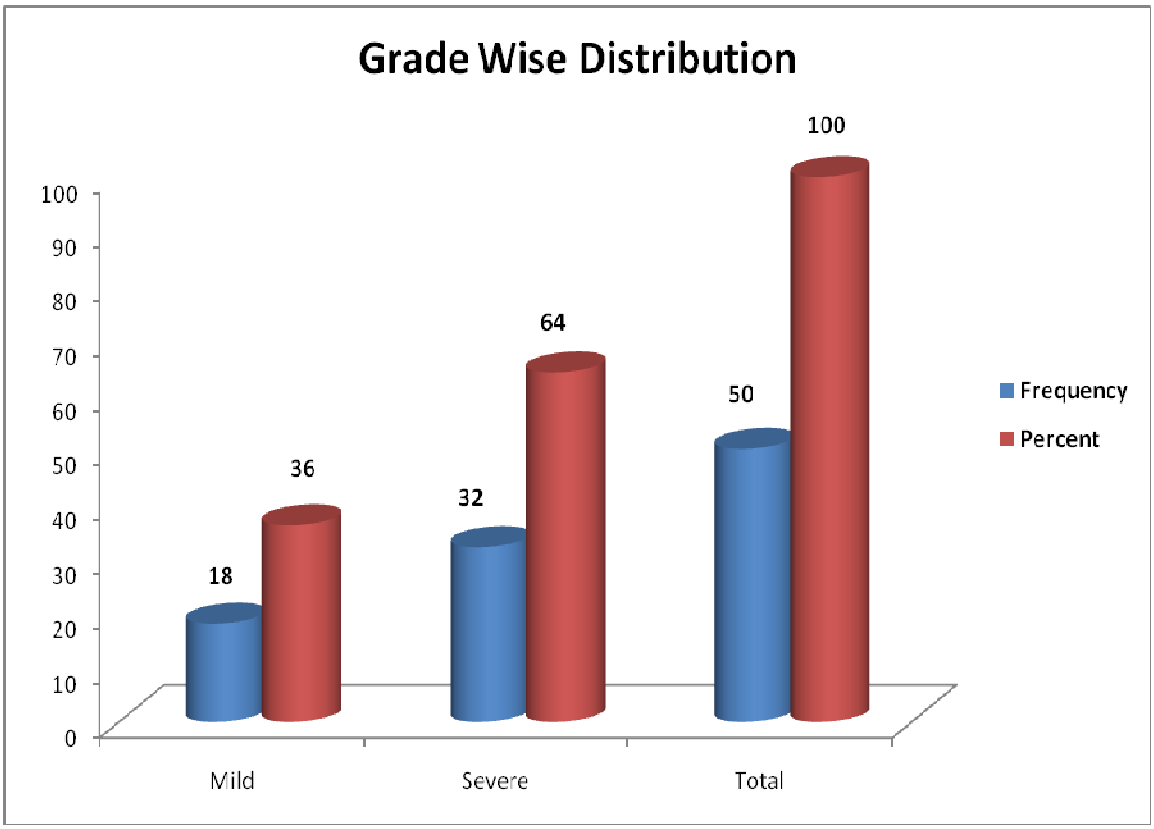


Table 5 : Haemoglobin levels distribution of study subjects:

Haemoglobin%	Frequency	Percent
Normal (>14 in M) (>13 in F)	11	22.0
Low	39	78.0
Total	**50**	**100.00**

Table 5 shows Anaemia found in 78% of acute pancreatitis patients .

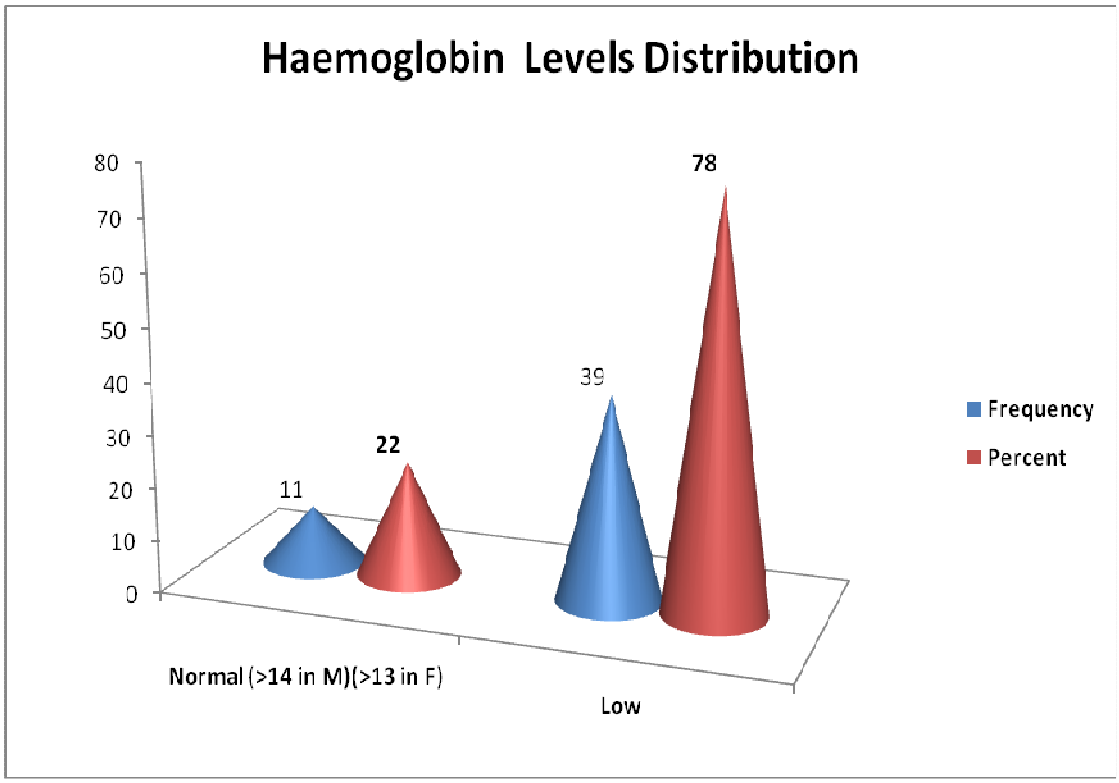


Table 6: Total count levels distribution of study subjects:

Total WBC Count	Frequency	Percent
Normal	38	76.0
<4000	2	4.0
>11000	10	20.0
Total	**50**	**100.00**

Table 6 shows Leukocytosis was seen in 20% of study subjects and leucopoenia found only in 4%.

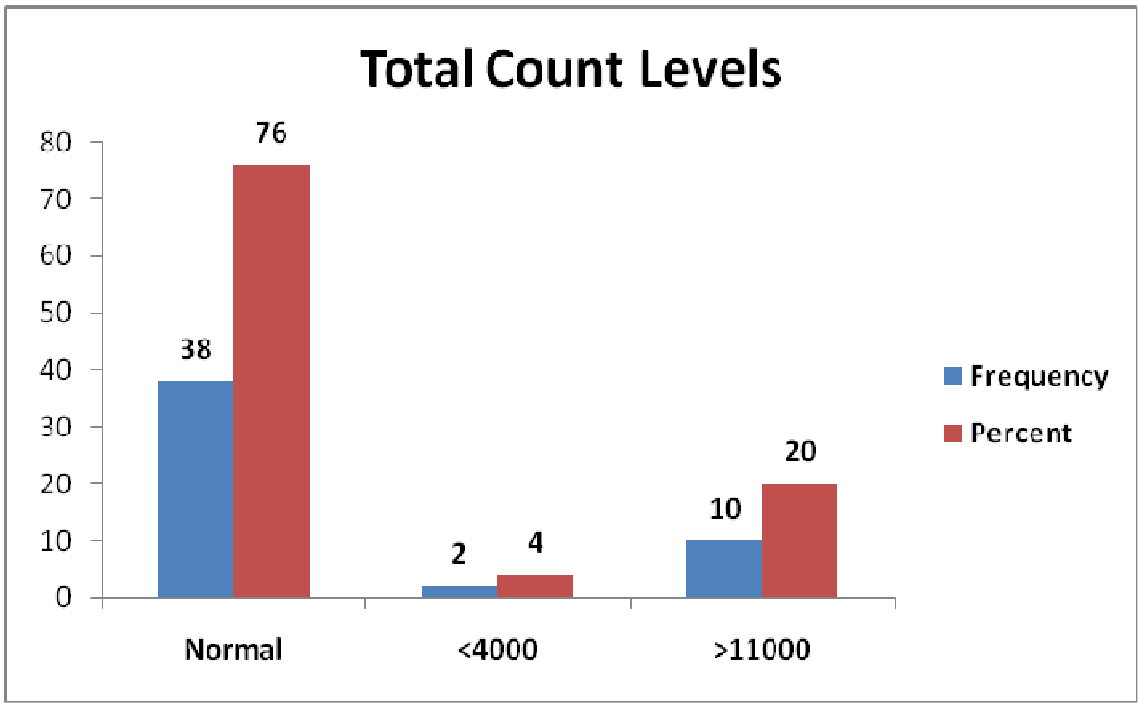


Table 7: Polymorph levels distribution of study subjects :

Polymorph%	Frequency	Percent
40-80%	35	70.0
<40%	1	2.0
>80%	14	28.0
Total	**50**	**100.00**

Table 7 shows Polymorph levels were higher in 28% of study population.

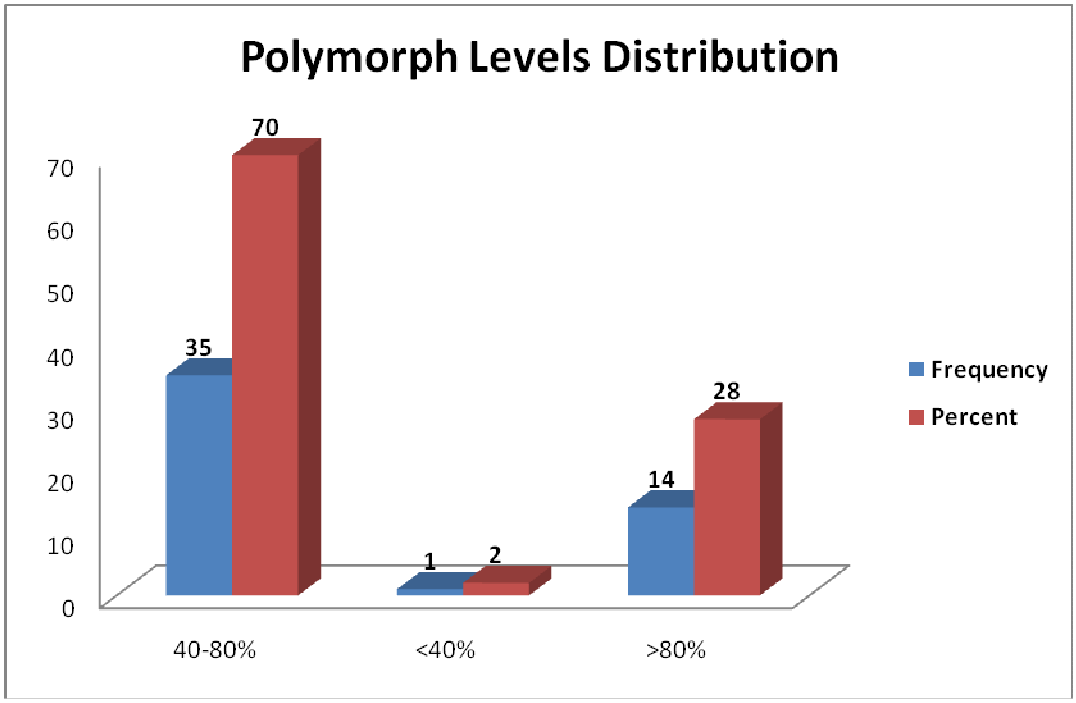


Table 8 :Haematocrit levels distribution of study subjects:

HCT%	Frequency	Percent
40-45%	9	18.0
<40%	38	76.0
>45%	3	6.0
Total	**50**	**100.00**

Table 8 shows Haematocrit levels were lower in 76% of patients ,where higher Haematocrit values seen only in 6%.

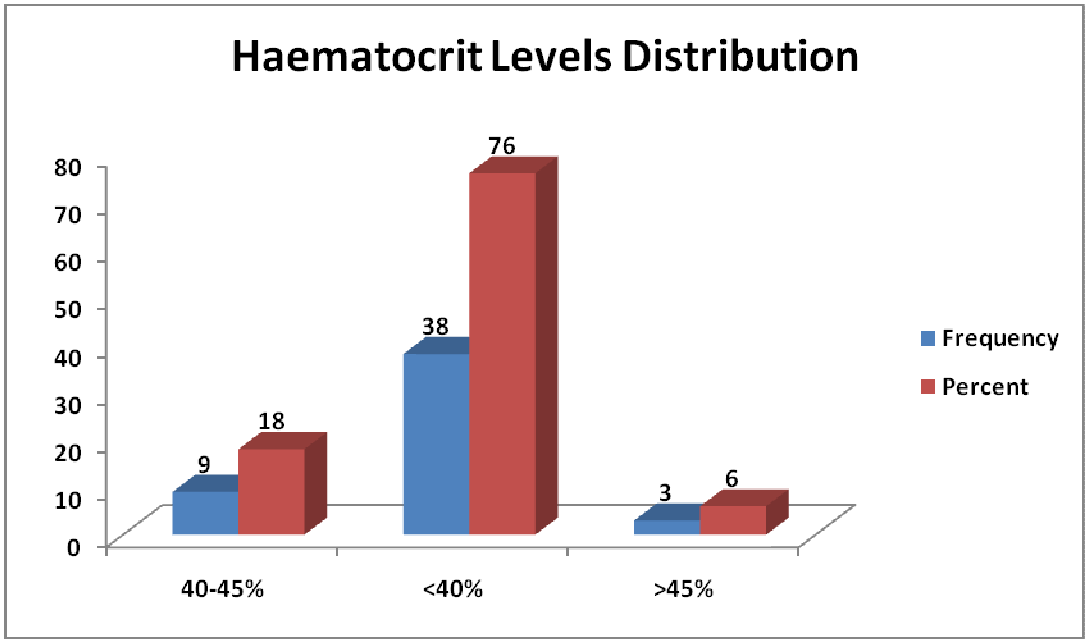


Table 9 : Platelet count levels distribution of study subjects :

Platelet Count level	Frequency	Percent
1.5to 4lakhs	30	60.0
<1.5lakhs	17	34.0
>4lakhs	3	6.0
Total	**50**	**100.00**

Table 9 shows Low platelets were found in 34% and high platelets observed in 6%.

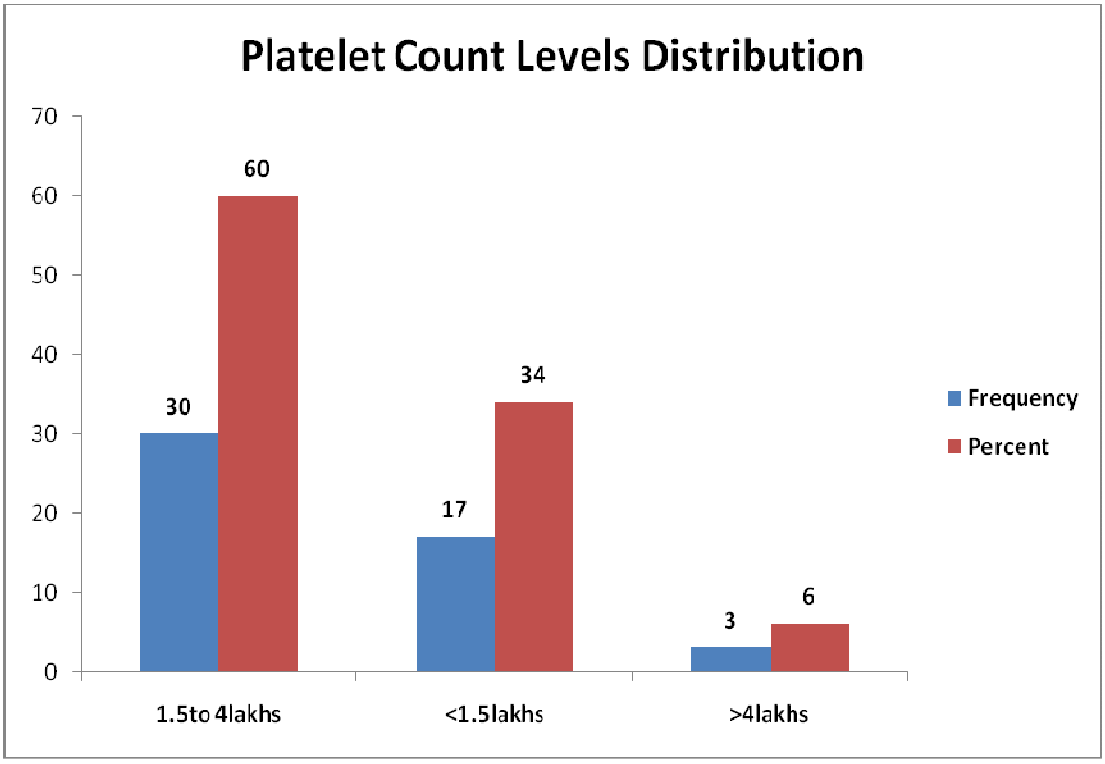


Table 10 : INR levels distribution of study subjects:

INR	Frequency	Percent
< 1.2	36	72.0
> 1.2	14	28.0
Total	**50**	**100.0**

INR levels were higher in 28% of study subjects.

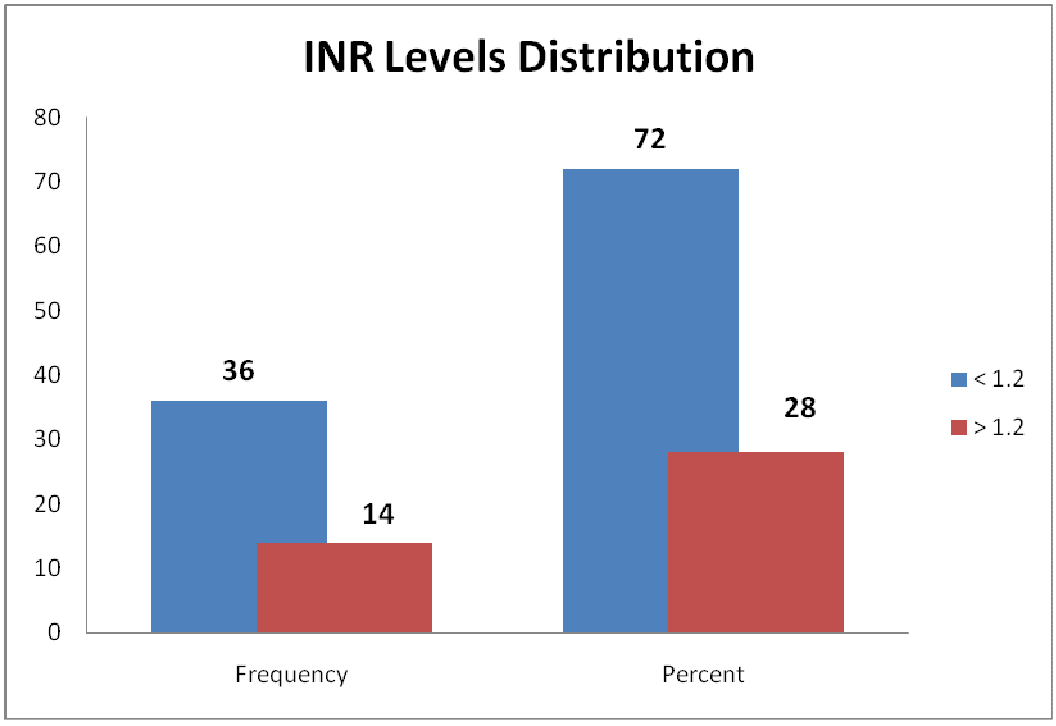


Table 11: APTT levels distribution of study subjects :

APTT	Frequency	Percent
24-36s	38	76.0
>36s	12	24.0
Total	**50**	**100.0**

Table 11 shows Increase in APTT levels in 24% of study population.

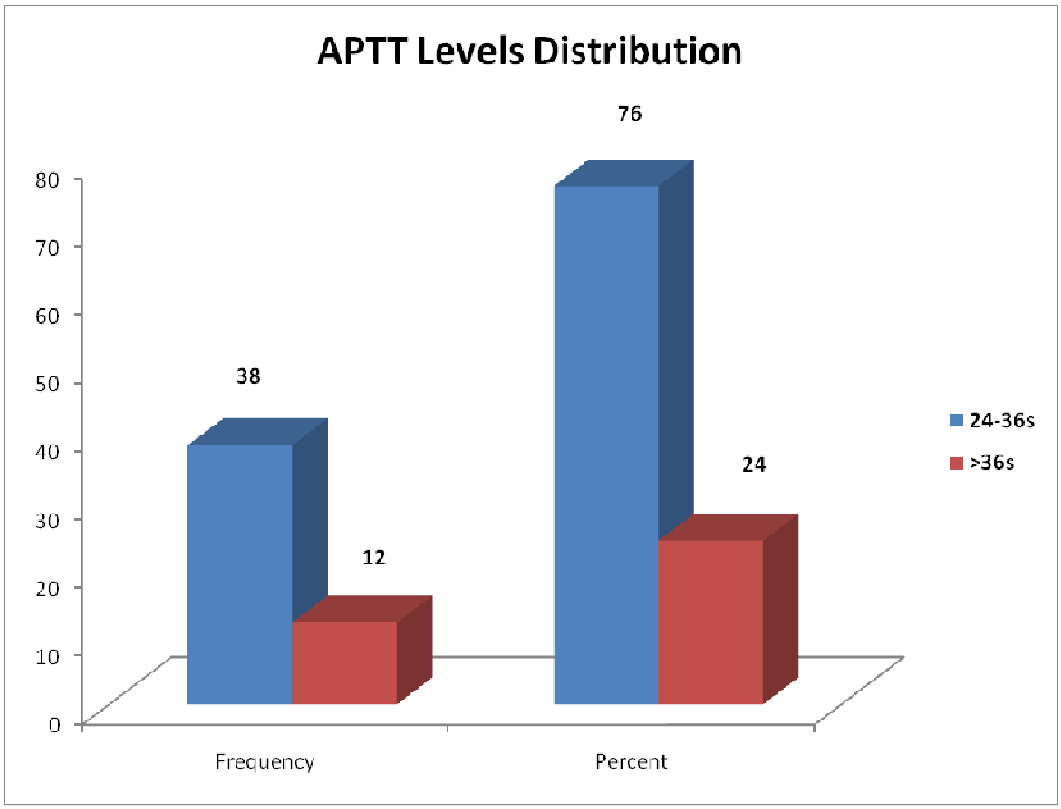


Table 12: Fibrinogen levels distribution of study subjects:

Fibrinogen	Frequency	Percent
180-350mg/dl	23	46.0
<180 mg/dl	8	16.0
>350mg/dl	19	38.0
Total	**50**	**100.0**

Table 12 shows Increase in fibrinogen levels in 38% and decrease in fibrinogen levels in 16%.

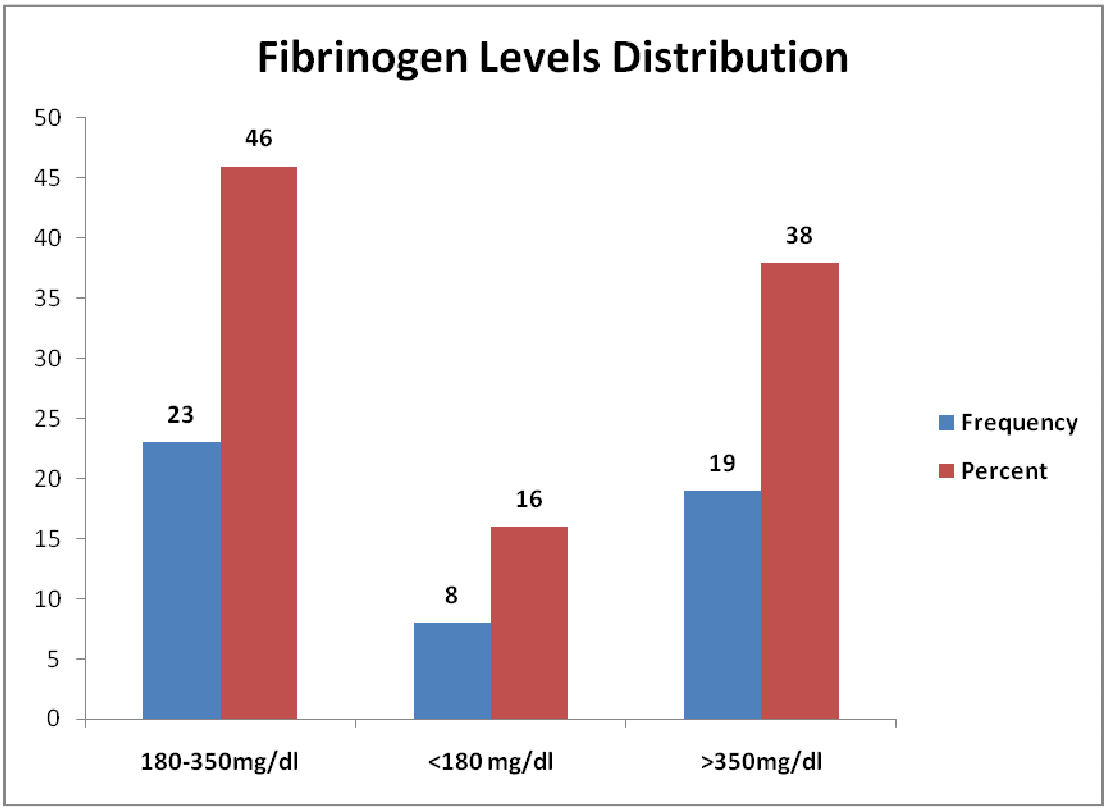
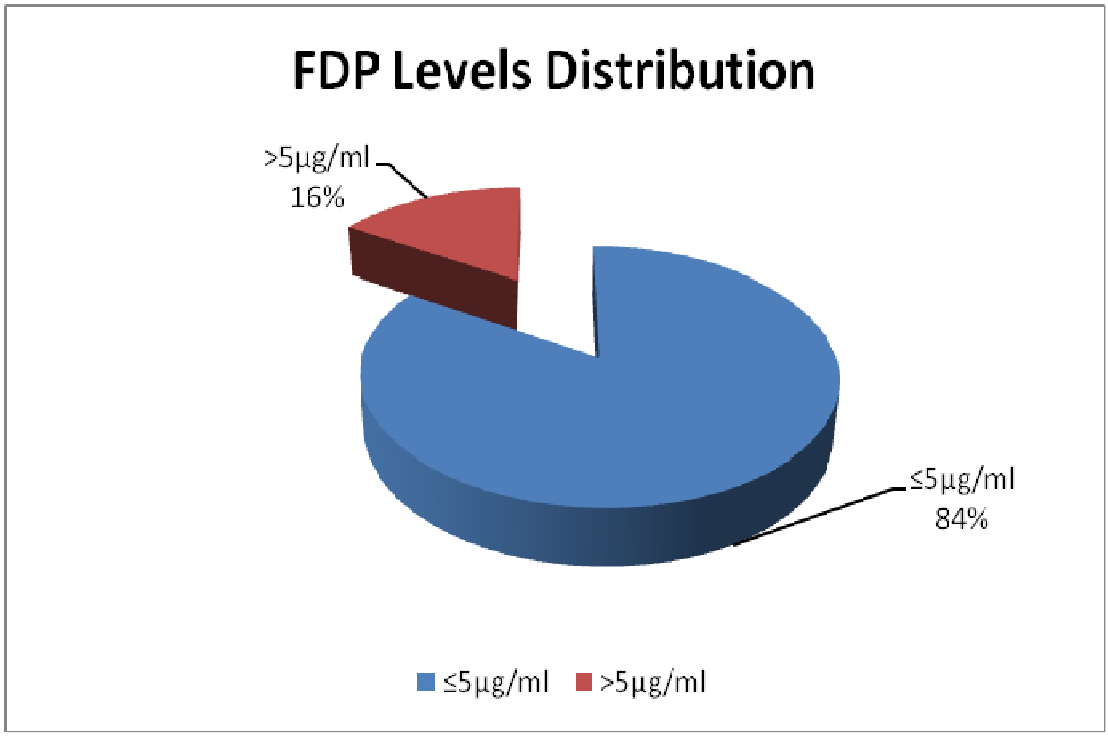


Table 13: FDP levels distribution of study subjects :

FDP	Frequency	Percent
≤5µg/ml	42	84.0
>5µg/ml	8	16.0
Total	**50**	**100.0**

Table 13 shows Increase in FDP levels in 16% of study subjects.



STATISTICAL ANALYSIS

Table- 1 Sex distribution in relation to Grade of acute pancreatitis

Sex Distribution		Grade		Total	Significance
		Mild	Severe		
Male	Count	15	29	44	Chi square
	% within Sex	34.1%	65.9%	100.0%	0.580
	% within Grade	83.3%	90.6%	88.0%	
Female	Count	3	3	6	P>0.05
	% within Sex	50.0%	50.0%	100.0%	Not significant
	% within Grade	16.7%	9.4%	12.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Sex	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Out of 44(88%) male patients ,29(90.6%) were in severe category and 15(83.3%) were in mild category.The observed difference between mild and severe category were not statistically significant(P>0.05)

Table 2- Age distribution in relation to grade of acute pancreatitis

Age Group in Years		Grade		Total	Significance
		Mild	Severe		
11-20	Count	1	3	4	Chi square
	% within Age Group in Years	25.0%	75.0%	100.0%	0.857
	% within Grade	5.6%	9.4%	8.0%	P>0.05
21-30	Count	4	10	14	Not significant
	% within Age Group in Years	28.6%	71.4%	100.0%	
	% within Grade	22.2%	31.3%	28.0%	
31-40	Count	9	12	21	
	% within Age Group in Years	42.9%	57.1%	100.0%	
	% within Grade	50.0%	37.5%	42.0%	
41-50	Count	3	4	7	
	% within Age Group in Years	42.9%	57.1%	100.0%	
	% within Grade	16.7%	12.5%	14.0%	
Above 50	Count	1	3	4	
	% within Age Group in Years	25.0%	75.0%	100.0%	
	% within Grade	5.6%	9.4%	8.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Age Group in Years	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Out of 50 study subjects, 32(64%) in severe category and 18(36%) in mild category. Patients belonging to age group from 11-40yrs presents more with severe category than patients age above 40years.Inspite of dominance of younger age group presenting with severe pancreatitis,the difference was not statistically significant(P>.05).

Table 3 Etiology wise distribution in relation to grade of pancreatitis:

Etiology		Grade		Total	Significance
		Mild	Severe		
Alcohol	Count	9	21	30	Chi square 0.725
	% within Etiology	30.0%	70.0%	100.0%	P>0.05 Not significant
	% within Grade	50.0%	65.6%	60.0%	
Gall Stones	Count	3	3	6	
	% within Etiology	50.0%	50.0%	100.0%	
	% within Grade	16.7%	9.4%	12.0%	
Hyper TGL	Count	1	1	2	
	% within Etiology	50.0%	50.0%	100.0%	
	% within Grade	5.6%	3.1%	4.0%	
Idiopathic	Count	5	7	12	
	% within Etiology	41.7%	58.3%	100.0%	
	% within Grade	27.8%	21.9%	24.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Etiology	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Alcohol accounts for 70% of severe pancreatitis group .In contrast in gall stone disease group 16.7% in mild group and 9.4% in severe group.But the difference between variables were not statistically significant.

Correlation of Haematological Parameters with Grade of pancreatitis :

Table 4:Haemoglobin variation with grade of Pancreatitis:

Hb		Grade		Total	Significance
		Mild	Severe		
Normal (<14 in M) (>13 in F)	Count	4	7	11	
	% within Hb	36.4%	63.6%	100.0%	Chi sq test
	% within Grade	22.2%	21.9%	22.0%	0.621
Low	Count	14	25	39	
	% within Hb	35.9%	64.1%	100.0%	P>0.05 Not significant
	% within Grade	77.8%	78.1%	78.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Hb	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Out of 50 study subjects, 32(78%) were anaemic in this study.But when these anaemic patients were compared with grade of pancreatitis,64.1% were in severe group and 35.9% in mild group the difference was not statistically significant (P>.05).

Table 5:Total Leukocyte count variation with grading of pancreatitis:

TC		Grade		Total	Significance
		Mild	**Severe**		
4000 - 11000	Count	16	22	38	
	% within TC	42.1%	57.9%	100.0%	Chi square
	% within Grade	88.9%	68.8%	76.0%	0.240
<4000	Count	0	2	2	P>0.05
	% within TC	.0%	100.0%	100.0%	
	% within Grade	.0%	6.3%	4.0%	
>11000	Count	2	8	10	
	% within TC	20.0%	80.0%	100.0%	
	% within Grade	11.1%	25.0%	20.0%	
Total	**Count**	**18**	**32**	**50**	
	% within TC	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Only 10(20%) of study subjects have leukocytosis in this study. Leukocytosis was found in 80% of severe type when compared with 20% of mild type.But the percentage within grade is 25% in severe group and 11.1% in mild group. Hence the difference was not statistically significant.

Table 6 : Polymorphs distribution in relation with grade of Acute pancreatitis:

Poly%		Grade		Total	Significance
		Mild	Severe		
40-80%	Count	13	22	35	Chi square
	% within Poly%	37.1%	62.9%	100.0%	0.747 P>0.05
	% within Grade	72.2%	68.8%	70.0%	
<40%	Count	0	1	1	Not significant
	% within Poly%	.0%	100.0%	100.0%	
	% within Grade	.0%	3.1%	2.0%	
>80%	Count	5	9	14	
	% within Poly%	35.7%	64.3%	100.0%	
	% within Grade	27.8%	28.1%	28.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Poly%	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Increase in Polymorphs seen more in severe acute pancreatitis(64.3%) than in mild acute pancreatitis (35.7%).But Polymorphs percentage within grade is 28.1% in severe acute pancreatitis and 27.8% in mild acute pancreatitis .Hence the difference was not statistically significant.(P>0.05).

Table 7 Haematocrit variation in relation with grade of acute pancreatitis:

HCT%		Grade		Total	Significance
		Mild	Severe		
40-45%	Count	3	6	9	Chi square
	% within HCT%	33.3%	66.7%	100.0%	
	% within Grade	16.7%	18.8%	18.0%	0.976
<40%	Count	14	24	38	P>0.05
	% within HCT%	36.8%	63.2%	100.0%	
	% within Grade	77.8%	75.0%	76.0%	Not significant
>45%	Count	1	2	3	
	% within HCT%	33.3%	66.7%	100.0%	
	% within Grade	5.6%	6.3%	6.0%	
Total	**Count**	**18**	**32**	**50**	
	% within HCT%	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Haemoconcentration (HCT>45%) which is a predictor of severe pancreatitis is seen only in 6%.Majority of the study subjects have decreased haematocrit values(76%).The difference was not statistically significant when the haematocrit values are compared with grade of pancreatitis.(P>0.05).

Table 8: Platelet count variation in relation to grade of pancreatitis:

Plt. Count		Grade		Total	Significance
		Mild	Severe		
Normal	Count	13	17	30	Chi square
	% within Pl.Count	43.3%	56.7%	100.0%	O.258
	% within Grade	72.2%	53.1%	60.0%	P>0.05
Low	Count	5	12	17	Not significant
	% within Pl.Count	29.4%	70.6%	100.0%	
	% within Grade	27.8%	37.5%	34.0%	
High	Count	0	3	3	
	% within Pl.Count	.0%	100.0%	100.0%	
	% within Grade	.0%	9.4%	6.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Pl.Count	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Thrombocytopenia is observed in 17 study subjects (34%) in this study. In these 17 patients, 12(70.6%) were in severe group and 5 (29.4%) in mild group. But percentage of thrombocytopenia within the grade was 37.5% in severe group and 27.8% in mild group and hence the differences was not statistically significant(P>0.05).

Table 9 : INR variation in relation to grade of acute pancreatitis:

INR		Grade		Total	Significance
		Mild	**Severe**		
<1.2	Count	13	23	36	Chi square
	% within INR	36.1%	63.9%	100.0%	0.979
	% within Grade	72.2%	71.9%	72.0%	P>0.05
>1.2	Count	5	9	14	Not significant
	% within INR	35.7%	64.3%	100.0%	
	% within Grade	27.8%	28.1%	28.0%	
Total	**Count**	18	32	50	
	% within INR	36.0%	64.0%	100.0%	
	% within Grade	100.0%	100.0%	100.0%	

14 (28%) study subjects showed Increase in INR values in this study. In this 14 study subjects 9 (64.3%) were in severe group and 5(35.7%) in mild group. But percentage of increase INR within grade was 28.1% in severe category and 27.8% in mild category and hence the difference was not statistically significant. (P>0.05)

Table 10 :APTT variation in relation to grade of acute pancreatitis :

INR		Grade		Total	Significance
		Mild	Severe		
Normal	Count	16	22	38	Chi square
	% within APTT	42.1%	57.9%	100.0%	0.109
	% within Grade	88.9%	68.8%	76.0%	P>0.05
High	Count	2	10	12	Not significant
	% within APTT	16.7%	83.3%	100.0%	
	% within Grade	11.1%	31.3%	24.0%	
Total	**Count**	18	32	50	
	% within APTT	36.0%	64.0%	100.0%	
	% within Grade	100.0%	100.0%	100.0%	

12 (24%) of study subjects have high APTT value and the value is more in severe pancreatitis group (83.3%) than in mild group (16.7%).But the percentage within the grade was 31.3% in severe group and 11.1% in mild group and the differences was not statistically significant.(P>0.05)

Table 11 : Fibrinogen variation in relation to grade of acute pancreatitis :

Fibrinogen		Grade		Total	Significance
		Mild	Severe		
Normal	Count	9	14	23	Chi Square
	% within Fibrinogen	39.1%	60.9%	100.0%	0.313
	% within Grade	50.0%	43.8%	46.0%	P>0.05
Low	Count	1	7	8	Not significant
	% within Fibrinogen	12.5%	87.5%	100.0%	
	% within Grade	5.6%	21.9%	16.0%	
High	Count	8	11	19	
	% within Fibrinogen	42.1%	57.9%	100.0%	
	% within Grade	44.4%	34.4%	38.0%	
Total	**Count**	**18**	**32**	**50**	
	% within Fibrinogen	**36.0%**	**64.0%**	**100.0%**	
	% within Grade	**100.0%**	**100.0%**	**100.0%**	

Out of 50 patients low fibrinogen observed in 8 (16%) and high fibrinogen observed in 19(38%) clients. Majority of low fibrinogenemia belongs to severe category (87.5%). Increase in fibrinogen levels are observed in 11(57.9%)patients in severe category and 8(42.1%)patients in mild category. The percentage difference between the above variables within grade was not statistically significant.(P>0.05)

Table 12: FDP variation in relation to grade of acute pancreatitis :

FDP		Grade		Total	Significance
		Mild	Severe		
Normal	Count	18	24	42	Chi square
	% within FDP	42.9%	57.1%	100.0%	0.021
	% within Grade	100.0%	75.0%	84.0%	P<0.05
High	Count	0	8	8	Significance at 5%
	% within FDP	.0%	100.0%	100.0%	
	% within Grade	.0%	25.0%	16.0%	
Total	Count	18	32	50	
	% within FDP	36.0%	64.0%	100.0%	
	% within Grade	100.0%	100.0%	100.0%	

High level of FDP observed in 8(16%) patients and all 8 cases were observed in severe category. Hence the difference between 2 grades were statistically significant (P<.05).

Table 13: Cross tabular variation between APTT and fibrinogen :

APTT		Fibrinogen			Total	Significance
		Normal	Low	High		
Normal	Count	20	4	14	38	Chi square
	% within APTT	52.6%	10.5%	36.8%	100.0%	0.104
	% within Fibrinogen	87.0%	50.0%	73.7%	76.0%	P>0.05
High	Count	3	4	5	12	Not significant
	% within APTT	25.0%	33.3%	41.7%	100.0%	
	% within Fibrinogen	13.0%	50.0%	26.3%	24.0%	
Total	Count	23	8	19	50	
	% within APTT	46.0%	16.0%	38.0%	100.0%	
	% within Fibrinogen	100.0%	100.0%	100.0%	100.0%	

This table shows that 4patients(33.3% within APTT) had rise in APTT value and decrease in fibrinogen.These patients can be considered as full blown DIC. 4 patients (50% within fibrinogen) have decrease in fibrinogen values but normal APTT values. These patients were early in development of DIC.The difference between 2 variables were not statistically significant (P>0.05).

Table 14: Cross tabular variation between APTT and FDP

APTT		FDP		Total	Significance
		Normal	High		
Normal	Count	33	5	38	Chi square
	% within APTT	86.8%	13.2%	100.0%	0.329
	% within FDP	78.6%	62.5%	76.0%	P>0.05
High	Count	9	3	12	Not significant
	% within APTT	75.0%	25.0%	100.0%	
	% within FDP	21.4%	37.5%	24.0%	
Total	Count	42	8	50	
	% within APTT	84.0%	16.0%	100.0%	
	% within FDP	100.0%	100.0%	100.0%	

This table shows 3 patients(25%within APTT) have both High APTT value and High FDP values indicative of DIC in these patients. 5 patients (62.5%within FDP) have High FDP values but normal APTT values, indicating that these patients were in early severe pancreatitis and feature suggestive of impending DIC. The difference between these two variables were not statistically significant.(P>0.05)

Table 15: Cross tabular variation between FDP and fibrinogen

FDP		Fibrinogen			Total	Significance
		Normal	Low	High		
Normal	Count	21	6	15	42	Chi square
	% within FDP	50.0%	14.3%	35.7%	100.0%	0.416
	% within Fibrinogen	91.3%	75.0%	78.9%	84.0%	P>0.05
High	Count	2	2	4	8	Not significant
	% within FDP	25.0%	25.0%	50.0%	100.0%	
	% within Fibrinogen	8.7%	25.0%	21.1%	16.0%	
Total	Count	23	8	19	50	
	% within FDP	46.0%	16.0%	38.0%	100.0%	
	% within Fibrinogen	100.0%	100.0%	100.0%	100.0%	

This table shows 2 patients(25%within FDP) have low fibrinogen levels and High FDP levels indicative of full blown DIC. 6 patients (75% within fibrinogen) have low fibrinogen values but normal FDP values implies these patients were in impending DIC.The difference between these 2 variables were not statistically significant(P>0.05).

DISCUSSION

Haematological and coagulation changes have been reported in acute pancreatitis as evidenced by Benjamin et al and Inner field et al in 1952,who did their study on coagulation changes in acute pancreatitis[8] and J.E . Trapnel et al in 1966 in journal of annals of Royal college of surgeons,England did study on Haematological changes in acute pancreatitis[1] and he reported drop in value of haematocrit and haemoglobin values and also reported significant leukocytosis in his study.

Acute Pancreatitis produces a severe inflammatory response which is mainly responsible for acinar cell damage which leads to release of inflammatory mediators like cytokines,TNF and PAF thereby resulting in a systemic inflammatory response[3].

These inflammatory mediators alter the normal hemostatic mechanism by acting in paracrine or autocrine loops to activate the monocytes,neutrophils to site of injury and these activated cells inturn expresses the tissue factor in the injured pancreatic cell and alter the coagulation pathway[8] .

The Hypothesis states that these coagulation changes may be due to early consumption of coagulation factors which are secondary to enzymes of pancreas , especially trypsin , or it may be secondary to vascular injury[5].

Hence recognition of these haematological and coagulation disturbance at earliest is essential especially disseminated intravascular coagulation to improve the outcome in patients with acute pancreatitis.

In this study, patients were graded in to mild and severe pancreatitis by Balthazar CT grade system/CTSI scoring system. After satisfying the inclusion and exclusion criteria , Haematological and coagulation changes were assessed in reference to these 2 grades.

Literature research showed that haematological abnormalities in acute pancreatitis were recorded in a prospective study by Desmond Murphy and Clement Imrie.

In another study by Li-Pe cheng ,he studied the influence of coagulation function on acute pancreatitis on 56 patients of acute pancreatitis with normal control group and found that the coagulation parameters were significantly increased indicating bad prognosis though the difference between the 2 groups were not statistically significant. In our study we found similar coagulation changes.

In our study, majority (88%)were male patients and most of patients belong to middle age group 28% and 42% for 21-30 and 31-40 age group respectively. The male predominance is due to the etiological factor which is alcohol abuse constituting about 60% of the study group. Though gall stones

are the next common etiological factor next to alcohol, in our study it constitutes about 12% only.

64% of patients belonged to severe pancreatitis group and 36% belonged to mild pancreatitis group. The haematological parameters and coagulation parameters were correlated with the 2 grades of acute pancreatitis and analyzed.

Haemoconcentration (HCT>45%) is a sign of severe acute pancreatitis[39]. However this was found only in 6% of our study group, where as decrease in haematocrit value were noted in 76%. This is due to the fact majority of patients in study group were anaemic.The Patients in our study group had haemoglobin level ranging from 6-12gms%.However the corresponding haematocrit was appreciably higher in most of the patients in severe acute pancreatitis indicating haemoconcentration.

Leukocytosis was noted in 20% of study group and they are found more (80%) in severe acute pancreatitis. Polymorphs were higher in 64.3% in severe group and 35.7% in mild acute pancreatitis.Although neutrophilic dominance is noted in 28 out of 32 patients with severe acute pancreatitis.4 had significant lymphocytosis affecting the P value . This is probably due to subclinical viral infection. Though these variables were more in severe pancreatitis,the

difference between these variables between mild and severe group were not statistically significant(P>0.05).

Thrombocytopenia was noted in 34% of study group,of which 70.6% were belong to severe acute pancreatitis.Thrombocytopenia could be due to a) a part of DIC with associated global prolongation of coagulation parameters or b) manifestation of thrombotic microangiopathy resulting from diffuse endothelial injury and platelet activation.

Prothrombin time was found to be increased in 28% of patients and was seen more in severe acute pancreatitis group(64.3%).Similarly increase in APTT values were seen in 24%,of which 83.3% were in severe pancreatitis group.

Fibrinogen levels were lower in 16% of study group, of which 87.5% was in severe pancreatitis group. These patients were in severe DIC. High fibrinogen values were seen in 38% ,of which severe pancreatitis accounts to 57.9%.These patients were in early stage of the disease and did not have frank haemostatic disturbance. This increased fibrinogen value in 38% of patients can be explained by the fact that fibrinogen is a acute phase reactant like CRP ,and hence can be increased with severe inflammation. Though these variables were more in severe pancreatitis,the difference between these

variables between mild and severe group were not statistically significant(P>0.05).

In contrast FDP levels were found to be higher in 16% of study group and all of them belong to severe group of pancreatitis. Hence the difference between these variables between mild and severe group were statistically significant (P<0.05%).

Cross tabulation done between APTT and fibrinogen values showed that 4patients(33.3% within APTT) had rise in APTT value with decrease in fibrinogen values .These parameters could indicate DIC in these patients. 4 patients (50% within fibrinogen) have decrease in fibrinogen values but normal APTT values. These patients can be early in development of DIC and these patients should receive more attention for better clinical outcome.

Similarly when cross tabulation was done between APTT and FDP, 3 patients(25%within APTT) have increased values of both APTT and FDP indicating DIC whereas 5 patients(62.5%within FDP) with high FDP value had normal APTT values.These patients presented in the early stage of severe acute pancreatitis and were probably with compensated DIC.Timely correction could avert progress to full blown DIC.

When fibrinogen and FDP was cross tabulated, 2 patients(25%within FDP) have features of full blown DIC with decrease in fibrinogen value and

increase in FDP values. 6 patients (75% within fibrinogen) have low fibrinogen values but with normal FDP values. Out of these 6 patients 5 were in severe category .It has been observed that the fibrinogen levels vary significantly in the first week of acute severe pancreatitis. Fibrinogen synthesis and lysis go hands together in acute pancreatitis depending on the inflammatory response.The natural anticoagulants (protein-C,AT-111) are also variably upregulated and downregulated by the acute phase reactants, essentially working against thrombosis. The fibrinogen and FDP values are therefore significantly influenced by inflammatory cytokines with variable thrombohaemorrhagic manifestations[53].

Though these crosstabulation variables with APTT,fibrinogen and FDP give clue about DIC and impending DIC developing in these patients, the difference between these variables between mild and severe group were not statistically significant($P>0.05$).

CONCLUSION

The study titled Prospective study on haematological and coagulation changes in acute pancreatitis was conducted in 50patients in Madras Medical college and Rajiv Gandhi Government general hospital,Chennai and following conclusions were made.

1. Haematological and coagulation abnormalities were more common in severe acute pancreatitis.

2. Though evidence of full blown Disseminated Intravascular Coagulation is seen in few patients, the cases which were impending Disseminated Intravascular Coagulation and cases which have high potential to develop Disseminated Intravascular Coagulation were recognised and could be managed effectively.

3. The difference between variables comparing haematological and coagulation indices with severity of pancreatitis were not statistically significant except for the increase in FDP value which was statistically significant .

4. Therapeutic regimens like Activated protein C ,Anti thrombin 111,Platelet activating factor modulating agents, Factor V11a inhibitors could be tried in near future to improve the clinical outcome of patients with severe coagulatory disturbance in acute pancreatitis.

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PROFORMA

Prospective study of Haematological and coagulation changes in Acute pancreatitis

Name: Age: Sex:

Address: Occupation:

Symptoms

- Abdominal pain
- vomiting
- abdominal bloatness
- abdominal distension
- Loss of appetite
- Weight loss

Past history:

- Diabetes mellitus
- Hypertension
- Previous h/o pancreatitis

Personal history:

- Smoking Alcoholism

General examination::

Pulse:

Blood Pressure:

Systemic Examination:

CVS: RS: Abdomen: CNS:

Investigations:

Blood :

Haemoglobin

Hematocrit

Total count

Differential count

RBC count

Reticulocyte count

Peripheral smear.

Platelet count

abdomen

ESR

Bleeding time

Clotting time

Prothrombin time/INR

Acitivated partial Thromboplastin time

Fibrinogen

Fibrinogen degradation Product

Urine:

Albumin

sugar

Deposit

Motion :

ova,cysts

Chest X ray PA view

ECG all leads

Ultrasonogram

CECT Abdomen

Serum Amylase

Serum Lipase

Fasting Lipid profile

Serum Calcium

Serum Phosphorus

Renal Function tests

Liver function tests

Sl No	Name	Age/Sex	G.E.No	S.Amylase U/L	S.Lipase U/L	CECT abd	chest Xray	Etiology	Modified CTSI/ Balthazar score	Grade
1	Mohan	39/M	1427/12	238	168	pesudocyst pancreas/inflammed pancreas	B/L PL.E	Alcoholic	CTSI-7/Gr D	Severe
2	Tamilselvan	16/m	1462/12	346	264	pesudocyst pancreas	Lt Pl.E	Idiopathic	CTSI-6/Gr D	Severe
3	Manikandan	19/M	1764/12	1112	678	Ascites/edematous pancreas	Lt Pl.E	Idiopathic	CTSI-6/Gr D	Severe
4	Babu	25/M	1843/12	521	161	Pesudocyst tail pancreas/bulky pancreas	Normal	Alcoholic	CTSI-6/Gr D	severe
5	Ponnusamy	34/M	1368/12	348	210	Peripancreatic fat stranding	Normal	Alcholic	CTSI-3/GrC	Mild
6	Malliga	40/F	1945/12	144.5	363.8	Bulky&edematous pancreas/fat stranding	Normal	gallstones	CTSI-2/GrC	Mild
7	Govindaraj	35/M	1398/12	538	184	Bulky pancreas/pseudocyst head &body	Rt PL.E/Pe.E	Alcoholic	CTSI-7/Gr D	Severe
8	Chakravarthy	35/M	2025/12	288	168	Bulky pancreas/collection pancreas head	Lt Pl.E	Alcoholic	CTSI-7/Gr D	Severe
9	Devi	28/F	1547/12	370	740	Bulky pancreas	Normal	Hyper TGL	CTSI-2/GrB	MIld
10	Prabhu	32/M	888/13	734	362	enlarged gland/Peripancreatic fat strand	Lt pl.E	Alcoholic	CTSI-7/Gr D	Severe
11	Sakunthala	55/F	1212/13	1369	344	Edematous pancreas/fluid collection head pancreas	Lt PL .E	Gallstones	CTSI-7/Gr D	severe
12	Bhagyaraj	28/M	1324/13	380	264	Pseudocyst tail/Lt psoas abscess	Lt PL .E	Alcholic	CTSI-8/GrE	severe
13	Ramesh	36/M	1892/12	368	520	Pseudocyst pancreas head and body	Rt PL.E	Alcoholic	CTSI-7/Gr D	severe
14	Kandasamy	30/M	1648/12	282	384	fluid collection head pancreas	Rt PL.E	alcoholic	CTSI-7/Gr D	severe
15	Mani	39/M	1005/13	332	374	Bulky&inflammed pancreas	Normal	Idiopathic	CTSI-3/GrC	mild
16	ranjith	27/M	890/13	216	450	fluid collection tail pancreas	Lt PL .E	Idiopathic	CTSI -6/Gr D	Severe
17	Sivashankar	24/M	1693/12	213.8	360.8	Pseudocyst pancreatic tail ,neck & liver	Lt Pl.E	Idiopathic	CTSI-7/Gr D	Severe
18	Adimoolam	38/M	1836/12	243	151.7	enlarged gland/Peripancreatic fat strand	Normal	Alcoholic	CTSI-3/GrC	mild
19	Dhanasekar	47/M	1114/13	146	220.8	enlarged gland/Peripancreatic fat strand	Normal	Alcoholic	CTSI-3/GrC	mild
20	Rajagopal	62/M	1323/13	226	320.8	body&tail bulky with peripancreatic fat stranding	B/L PL.E	Alcoholic	CTSI-7/Gr D	Severe
21	Shankaraiah	48/M	1114/13	182	470	pseudocyst body and tail	Lt PL.E	Alcoholic	CTSI-8/GrD	Severe
22	Thimmaram	37/M	1674/13	1340	7350	Bulky pancreas/choledocholithiasis	Rt PL.E	Gall stone	CTSI-7/Gr D	Severe
23	Abdul majith	49/M	2122/13	197.86	169.2	Pseudocyst pancreas head/bulky edematous	Lt Pl.E	Alcoholic	CTSI-7/Gr D	Severe
24	Nagamuthu	47/M	2094/13	115.48	139	Bulky pancreatic head/peripancreatic fat strands	Normal	Alcoholic	CTSI-3/GrC	mild
25	Gopinath	31/M	1387/12	222	184	Bulky pancreas	Normal	Alcoholic	CTSI-3/GrC	mild
26	Janarthanan	48/M	1098/13	535	380	Bulky pancreas/ascites	Lt Pl.E	Alcoholic	CTSI-6/Gr D	Severe
27	Harikrishnan	54/M	1849/12	1425.4	412	Pseudocyst head& uncinate process	Lt PL.E	Alcoholic	CTSI-7/Gr D	severe
28	Devaraj	45/M	2056/13	1834	294	Marginal irregularity head&uncinate pancreas	Rt PL.E	Idiopathic	CTSI-3/GrC	mild
29	Saravanan	28/M	1486/12	354	627	Edematous pancreas	B/L PL.E	Alcoholic	CTSI-6/Gr D	severe
30	Manikandan	14/M	1406/12	3174	295	Edematous pancreas	Normal	Idiopathic	CTSI-3/GrB	mild
31	Allimuthu	28/M	1308/13	398	340	edematous pancreas/peripancreatic fat stranding	Normal	Idiopathic	CTSI-3/Gr C	mild
32	Prakash	29/M	1108/13	365	3678	edematous pancreas/peripancreatic fat stranding	Lt PL.E	alcoholic	CTSI-7/Gr D	severe
33	Moorthy	34/M	468/13	119	256	Psuedocyst body and tail	Rt Pl.E	Alcoholic	CTSI-7/Gr D	severe

34	Elango	31/M	2147/12	251	158	Bulky pancreas /Peripancreatic fluid collections	Lt Pl.E	Alcoholic	CTSI-7/Gr D	severe
35	Ramesh	38/M	1597/12	600	258	edematous pancreas/calculus in GB	Normal	Gall stone	CTSI-3/Gr C	mild
36	Varadharajan	51/M	2118/12	1579	327	edematous pancreas/peripancreatic fat stranding	normal	Idiopathic	CTSI-4/GrC	mild
37	Vinoth	30/M	1892/12	354	226	stones in GB & CBD/peripancreatic fat stranding	Normal	Gall stone	CTSI-4/GrC	mild
38	Anand	25/M	2008/13	4231	252	bulky pancreas/pancreatic ascites	Lt Pl.E	Idiopathic	CTSI-6/Gr D	severe
39	Rajesh	22/M	1643/13	243	182	Bulky and edematous pancreas	Normal	alcoholic	CTSI-3/Gr C	mild
40	Anandhan	38/M	1204/13	147	176	bulky pancreas/peripancreatic fat stranding	Normal	Idiopathic	CTSI-3/GrC	mild
41	Shakunthala	32/F	1311/13	228	426.4	edematous pancreas/peripancreatic fat stranding	B/L PL.E	Idiopathic	CTSI-7/Gr D	severe
42	Karunakaran	39/M	1845/12	102	144	bulky pancreas/peripancreatic fat stranding	B/L PL.E	Alcoholic	CTSI-7/Gr D	Severe
43	Kashif	18/M	1074/13	168	282	Pseudocyst Head of pancreas	Lt Pl.E	Idiopathic	CTSI-6/Gr D	Severe
44	Sampath	47/M	2114/12	542	468	pseudocyst body and tail	Lt PL.E	Alcoholic	CTSI-7/Gr E	Severe
45	Kavitha	32/F	1809/12	282	346	Fluid collection in peripancreatic region/lesser sac	Lt Pl.E	Hyper TGL	CTSI-8/GrE	Severe
46	Pushpa	36/F	1467/12	144	382	Bulky and edematous pancreas	Normal	Idiopathic	CTSI-3/GrB	mild
47	Saravanan	38/M	1348/12	118	260	Peripancreatic fat stranding	Normal	Alcoholic	CTSI-4/GrC	mild
48	Manikandan	28/M	1690/13	230	990	bulky pancreas with peripancreatic fluid	Lt Pl.E	Alcoholic	CTSI-7/GrD	severe
49	Prabhakaran	39/M	1963/12	210	260	emphysematous pancreatitis/distal CBD calculus	B/L PL.E	gallstone	CTSI-7/GrD	severe
50	Vadivel	29/M	2204/12	528	416	Peripancreatic fat stranding/pseudocyst head	Lt Pl.E	Alcoholic	CTSI-6/Gr D	severe

Sl No	Name	Age/Sex	G.E.No	Hb gm%	TC in %	DC in %	HCT in %	ESR 1hr	RBC count Mill/cu mm	Pl.count Lakh/cumm	Reticulocyte count	Peripheral smear	BT	CT	PT/INR	APTT secs	Fibrinogen mg/dl	FDP µg/ml
1	Mohan	39/M	1427/12	8.9	10,700	P90L7E3	27	40	3.4	2.07	1.50%	N N	2mts 40s	6mts 15s	15.5/1.12	37	741	5
2	Tamilselvan	16/m	1462/12	9.8	2 700	P68L32	32%	36	4.3	78,000	0.20%	M H	2mt	5mts 10s	14/1.0	26.5	324.8	<5
3	Manikandan	19/M	1764/12	6.6	18,150	P76L20E4	28%	45	5.11	4.08	0.40%	MH	2mts 10s	5mts	12.2/1.15	33.7	364.7	10
4	Babu	25/M	1843/12	11.1	3800	P70L27E3	34	20	4	93000	0.50%	NN	3mt 20s	6mt 15s	16.5/1.56	28.2s	368.2	5
5	Ponnusamy	34/M	1368/12	10.3	10,200	P80L18E2	30	34	3.56	2.60lakhs	2%	MH	2mts 30s	6mts 30s	16.0/1.5	37.9s	224.4	<5
6	Malliga	40/F	1945/12	11.9	15,800	P96L6E2	35	20	4.35	3.18	0.30%	NN with MH	3mts 20s	7mts 20s	12.3/0.88	30.3s	450	5
7	Govindaraj	35/M	1398/12	8	12,900	P80L12 E8	25	40	2.55	4.07	0.50%	MH	3mts45s	5mts 30s	13.7/0.98	49.2	382	5
8	Chakravarthy	35/M	2025/12	10.2	7 300	P73L1E12	30	26	3.48	3.76	0.80%	NNwith MH	3mts 20s	5mts 15s	NC	NC	397	>5
9	Devi	28/F	1547/12	9.6	8,000	P51L47E2	30	42	3.7	95000	0.10%	MH	2mt 10s	3mts45s	12.2/1	27.2s	324.6	<5
10	Prabhu	32/M	888/13	6	16,800	P88L7E5	17	62	3.14	2.03	0.50%	MH/leukocytosis	3mts 15s	5ts 45s	12.6/1.08	35s	380.7	5
11	Sakunthala	55/F	1212/13	11.3	5,200	P70L29E1	36	25	4.2	2.37	0.70%	MH/atyp Lymp	1mt30s	7mt15s	NC	NC	103.5	5
12	Bhagyaraj	28/M	1324/13	8	14 200	P85L10E5	32	26	3.37	3.11	1.00%	MH	2mts 30s	6mts 20s	14.3/1.11	42.3	505.6	5
13	Ramesh	36/M	1892/12	9	8,900	P87L9E4	27	34	3.37	1.3	0.80%	NN	3mts 20s	5mts40s	12.6/1.08	28	186.4	<5
14	Kandasamy	30/M	1648/12	14.3	9,100	P60L36E4	42	8	4.33	2.24	0.70%	MH	3mts 40s	6mts 20s	16.0/1.5	36	184.2	>5
15	Mani	39/M	1005/13	13.2	6 200	P62L30E8	39	5	3.38	3.16	0.80%	NN	2mts 40s	mts 30s	15.0/1.36	33	398	<5
16	ranjith	27/M	890/13	14.5	13,610	P85L12E3	42.4	6	5.1	2.45	0.80%	NN mild Leu ↑	1mt 30s	4mts10s	14.9/1.34	38.2	320.3	<5
17	Sivashankar	24/M	1693/12	4.5	5,500	P60L33E7	42	4	5.11	2.91	0.10%	Normal	1mt 33s	2mt44s	12.2/1.0	29.0s	207	5
18	Adimoolam	38/M	1836/12	8.9	4,900	P90L8E2	42	42	2.99	1.88	0.80%	Normal	2mt 07s	3mt 12s	12.6/1.08	36	320.8	<5
19	Dhanasekar	47/M	1114/13	9	10,200	P57L41E2	30	22	4.2	1.44	0.50%	NN	3mts 08s	6mts 30s	16.5/1.56	42.3	690.7	5
20	Rajagopal	62/M	1323/13	11	9,500	P75L22 E3	33	22	3.48	80,000	0.80%	MH/aty Lymp	1mt 48s	4mt20s	12.2/1	35s	<50	5
21	Shankaraiah	48/M	1114/13	10.6	15,200	P80L18E2	34	22	3.7	4.21	0.50%	NN with MH	2mt 30s	5mt40s	16.0/1.5	34s	342	<5
22	Thimmaram	37/M	1674/13	12.6	7,800	P81E2B1L16	29.7	50	5.12	92,000	0.80%	NN ,Target cells	2mt 30s	3mt50s	22.2/2.05	46.2	93	5
23	Abdul majith	49/M	2122/13	12	9,200	P67L26E7	26	68	4.26	1.8	0.80%	NN	1mt 10s	3mt50s	14.3/1.11	39.2	179.5	10
24	Nagamuthu	47/M	2094/13	8.4	11,000	P70L25E5	26	46	5.36	2	0.50%	NN with MH	1mt10s	3mt 20s	12.6/1.08	28.5	320	<5
25	Gopinath	31/M	1387/12	9.6	9,800	P51L45E4	32	42	3.46	1.82	0.80%	NN with MH	3mt 15s	5mt40s	12.6/1.08	32.4	126.2	<5
26	Janarthanan	48/M	1098/13	13.9	7,700	P70L27E3	38.2	9	3.92	3	0.80%	MH	1mt52s	3mts20s	12.2/1.0	36s	316.8	<5
27	Harikrishnan	54/M	1849/12	4.6	5,500	P70L22E8	15	28	2.24	2.06	0.70%	NN	2mt 30s	5mts 30s	12.6/1.08	34s	282.8	>5
28	Devaraj	45/M	2056/13	14.6	14,300	P79L11E1	41.7	20	4.29	254,000	0.80%	MH	3mts 30s	4mts 20s	14.3/1.11	36	182.3	<5
29	Saravanan	28/M	1486/12	14.7	10,600	P90L8E2	43	10	5.54	1.19	0.70%	NN mild Leu ↑	3mts 40s	5mts 30s	14.9/1.34	30	282.4	5
30	Manikandan	14/M	1406/12	8.5	11,100	P70L25E5	26	42	3.86	2	0.80%	MH	3mts 45s	5mts 20s	12.6/1.08	32	380.6	<5
31	Allimuthu	28/M	1308/13	16.8	10,200	P88L6E6	50	10	6.06	1.45	0.70%	NN MH	4mts	6mts	12.6/1.08	36s	383.2	5
32	Prakash	29/M	1108/13	12	7,100	P35L60E7	36.6	46	4.52	3	0.80%	NN mild Leu ↑	3mts 10s	5mts 10s	14.3/1.11	38s	342.5	<5
33	Moorthy	34/M	468/13	15.4	7,600	P70L28E2	49	28	4.66	1.22	0.50%	Normal	3mts15s	6mts 15s	14.2/1.11	36	124	<5
34	Elango	31/M	2147/12	13.4	6,700	P80L19E1	40	20	5	2	0.60%	Normal	2mts 07s	5mts 12s	12.2/1.0	28	128.2	<5
35	Ramesh	38/M	1597/12	11.7	7,500	P87L11E2	35	26	3.75	1.27	0.80%	MH	3mts 20s	4mts 20s	12.6/1.08	30	324.2	<5

36	Varadharajan	51/M	2118/12	14.5	9,300	P77L15E8	36	35	4.56	3	0.80%	NNwith MH	3mts 08s	6mts 20s	15.0/1.36	32s	362.4	5
37	Vinoth	30/M	1892/12	10.9	5,800	P75L20E5	35	25	3.6	3.1	0.70%	MH	3mts24s	5mts 30s	14.9/1.25	33.6	380.4	5
38	Anand	25/M	2008/13	11.8	10,900	P87L6E3	35	30	4.39	1	1.50%	NN	4mts20s	6mts 20s	14.3/1.11	30s	383.2	5
39	Rajesh	22/M	1643/13	18.8	5,100	P70L26E4	42	8	5.03	1.43	0.50%	NN	1mt 40s	3mts 20s	12.6/1.08	36	268.4	<5
40	Anandhan	38/M	1204/13	12.3	11,000	P87L10E3	36	15	3.87	3	1.00%	NN	2mt 13s	4mts38s	12.3/0.88	32.4s	362.4	<5
41	Shakunthala	32/F	1311/13	8.7	11 500	P68L26E6	27	22	4.22	1.01	0.80%	MH Aty Lym/eos	1mt 30s	7mts15s	16.0/1.5	38s s	103.5	>5
42	Karunakaran	39/M	1845/12	10.5	6,900	P60L38E2	33	25	3.88	2	0.50%	NN	1mt40s	3mt 49s	12.8/1.16	36s	328	<5
43	Kashif	18/M	1074/13	14	8,300	P81L17E2	42	8	5.2	1.57	0.60%	MH	2mts 32s	4mts 28s	12.6/1.08	34.8s	382	5
44	Sampath	47/M	2114/12	16	7,000	P59L35E6	48	4	4.88	2	0.70%	NN	1mt45s	5mts 35s	14.3/1.11	36s	278	<5
45	Kavitha	32/F	1809/12	12.8	4,000	P64l26 E10	42	18	3.9	30000	0.30%	MH	1mt 20s	3mt 40s	12.2/1.0	32	435	20
46	Pushpa	36/F	1467/12	9.4	5 300	P60L35E5	35	20	4.2	3	0.20%	MH	2mts 30s	4mts 20s	14.3/1.11	36	326	<5
47	Saravanan	38/M	1348/12	8.98	5,700	P71L26E3	29	28	3.9	2.65	0.60%	NN	2mt10s	4mts 30s	12.6/1.08	32.2s	286.8	<5
48	Manikandan	28/M	1690/13	12.4	5,200	P40L54E6	37	8	4.08	3	0.20%	MH/Plt↑	1mt15s	3mts 40s	14.5/1.04	26.4s	321.4	<5
49	Prabhakaran	39/M	1963/12	10.2	6,360	P67L30E3	28	32	3.24	1.16	0.50%	NN	2mts 30s	4mts 20s	15.3/1.10	16.6	613.7	10
50	Vadivel	29/M	2204/12	8.7	15,900	P80L8E2	26	30	3.86	86,000	0.50%	MH	3mts 20s	6mts 20s	14.3/1.1	24.8	320.8	<5

eys for Master Chart

Normal Values

Haemoglobin	-	Men : 14+ Female 13+
Total Count	-	4000 to 11000
Differential Count	-	Polymorph : 40-80% Lymphocytes : 20-40%
		Monocytes : 2-10% Eosinophils : 1-6%
		Basophils : <2%
Haematocrit	-	40-45%
Platelet Count	-	1.5 to 4 lakhs
ESR	-	>15
Recticulocyte count	-	<1.5%
Prothrombin Time	-	>3 sec.
INR	-	>1.2
Fibrinogen	-	180-350
FDP	-	<5

Abbreviation of Master Chart

Peripheral Smear	-	MH-Microcytic Hypochromic
NN	-	Normocytic Normochromic
Pl.E	-	Pleural Effusion.
CTSI	-	Computerised tomography severity index
GE.No	-	Gastroenterology number

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.A. Shafique
PG in DM Medical Gastroenterology
Madras Medical College, Chennai -3

Dear Dr.A. Shafique

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Prospective study on Hematological and coagulation changes in Acute pancreatitis " No.15042012.

The following members of Ethics Committee were present in the meeting held on 19.04.2012 conducted at Madras Medical College, Chennai -3.

1.	Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3.	Prof. B. Kalaiselvi MD Prof. of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Inst. of Internal Medicine, MMC, Ch-3	-- Member
5.	Prof. Md. Ali. MD.DM Prof & HOD, Dept. of MGE, MMC, Ch-3	-- Member
6.	Prof.P.Karkuzhali MD Director i/c, Prof., Inst. of Pathology. MMC, Ch-3	-- Member
7.	Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
8.	Prof. A. Radhakrishnan MD Prof of Internal Medicine, MMC, Ch-3	-- Member
9.	Thiru. S. Govindsamy. BABL	-- Lawyer
10.	Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

கணைய அழற்சியினால் ஏற்படும் குருதி மாற்றங்கள் மற்றும் திறள்வு மாற்றங்கள் பற்றிய ஆய்வு.

ஆராய்ச்சி நிலையம் : வயிறு மற்றும் குடல் சார்ந்த மருத்துவப் பிரிவு,
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை மற்றும்
சென்னை மருத்துவக் கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் : உறவுமுறை :

பங்கு பெறுபவரின் எண். :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லாத எதிர்பாராத வழக்கத்திற்கு நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு இரத்தத்தில் பரிசோதனை செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம்..... இடம்..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம்..... இடம்..... தேதி

ஆய்வாளரின் பெயர்.....

ஆராய்ச்சி தகவல் தாள்

இராஜீவ் காந்தி அரசு பொது மருத்துவமனைக்கு கணைய அழற்சி பாதிப்புடன் வரும் நோயாளிகளிடம் இந்த ஆய்வு நடைபெறுகிறது.

கணைய அழற்சி உள்ள நோயாளிகள் அனுமதிக்கப்பட்ட பிறகு அவர்களுக்கு, குருதி மாற்றங்கள் மற்றும் திறள்வு மாற்றங்கள் எத்தகைய தன்மையில் உள்ளது என்று அறிவதே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி :

INFORMATION SHEET

- We are conducting a prospective study on haematological and coaguation changes in acute pancreatitis in patients admitted in the ward at Rajiv Gandhi Government &general hospital with clinical features and investigations suggestive of acute pancreatitis.
- The purpose of the study is to analyze the haematological and coagulation changes in acute pancreatitis who are admitted with clinical features and investigation suggestive of acute pancreatitis and correlating the changes to its severity .
- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary.You are free to decide whether to participate in this study or to withdraw at any time;your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

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Paper ID	312031570
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E-mail	shafuss@yahoo.in
Submission time	20-Mar-2013 05:07PM
Total words	7871

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PROSPECTIVE STUDY ON HAEMATOLOGICAL AND COAGULATION CHANGES IN ACUTE PANCREATITIS Dissertation submitted in partial fulfillment of the requirements for the award of the degree of DM(MEDICAL GASTROENTEROLOGY) BRANCH - IV of THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI, INDIA. MADRAS MEDICAL COLLEGE, CHENNAI 600003 August 2013 INTRODUCTION Acute pancreatitis was defined in the Atlanta symposium as an acute inflammatory process involving the pancreas that further involve peripancreatic tissues and organs remote from the pancreas. Criteria had been defined for severity which include organ failure (Pulmonary insufficiency,shock and renal failure) and /or complications involving locally...

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